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Access DB# 9/344

SEARCH REQUEST FORM

Scientific and Technical Information Center

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Requester's Full Name: SHAM	ION FOLEY	Examiner #: 77851 Date: 9/10/3	••
Art Unit: 1648 Phone N	Number 30 8-3983	Serial Number: 09/925 635	
Mail Box and Bldg/Room Location	n: 88/6/8/309 Resu	Ilts Format Preferred (circle): PAPER DISK E-MA	.lL
If mor than one search is subm	itted, please prioritiz	e searches in order of need. MEI	***
		as specifically as possible the subject matter to be searched.	
	that may have a special me	yms, and registry numbers, and combine with the concept or raning. Give examples or relevant citations, authors, etc, if abstract.	
	//		
Title of Invention: Novel gount			/
Inventors (please provide full names):	1knna Kristasen	SONI; Jame Uldal AMHBEN;	
. Stig Hasmul-Olsen + L	isc CLIND	·	
Earliest Priority Filing Date:	8 /9/00	_<	_
For Sequence Searches Only Please includ	de all pertinent information (p	parent, child, divisional, or issued patent numbers) along with the	i
appropriate serial number.		./	
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- Biotechnology & Chemical L	Library	So no Ollar Stack is I gold	
CM1 1E07 - 703-308-449 jan.delaval@uspto.gov	1	(Just water you to save time.)	
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STAFF USE ONLY	Type of Search	Vendors and cost where applicable	
Searcher:	NA Sequence (#)	STN	
Searcher Phone #:	AA Sequence (#)	Dialog	
Searcher Location:	Structure (#)	Questel/Orbit	
Date Searcher Picked Up: 4/29/3	Bibliographic	Dr.Link	
Date Completed: 4124 (53	Litigation	Lexis/Nexis	*
Searcher Prep & Review Time:	Fulltext	Sequence Systems	
Clerical Prep Time:	Patent Family	WWW/Internet	
		w w w/internet	

PTO-1590 (8-01)

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mary.hale@uspto.gov.



The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact *the BioTech-Chem searcher* who conducted the search *or contact*:

Mary Hale, Supervisor, 308-4258 CM-1 Room 1E01

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I am an examin	er in Workgroup: (Example: 1610)
> Relevant prior	art found, search results used as follows:
	rejection
<u> </u>	rejection
Cite	d as being of interest.
. Help	bed examiner better understand the invention.
☐ Help	ped examiner better understand the state of the art in their technology.
Types of rel	evant prior art found:
☐ Fore	eign Patent(s)
☐ Nor (jou	n-Patent Literature nal articles, conference proceedings, new product announcements etc.)
> Relevant prio	r art not found:
□Resi	ults verified the lack of relevant prior art (helped determine patentability).
	ch results were not useful in determining patentability or understanding the invention
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d 189 all hitstr tot
    ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2003 ACS
T.89
     2002:927212 HCAPLUS
ΑN
     138:8313
DN
     Solid form immunity adjuvant and vaccine containing
ΤI
     Dupuis, Laurent; Ganne, Vincent; Aucouturier, Jerome; Trouve, Gerard
IN
     Societe D'exploitation De Produits Pour Les Industries Chimiques - Seppic,
PA
SO
     PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT
     Patent
LA
    French
IC
    A61K009-00
CC
     63-3 (Pharmaceuticals)
FAN.CNT 1
                                           APPLICATION NO.
                                                            DATE
     PATENT NO.
                      KIND DATE
     ______
                      ____
                            _____
                                           WO 2002-FR1775
                                                            20020527
                            20021205
PΙ
     WO 2002096386
                       Α1
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
                                           FR 2001-7149
                                                            20010531
     FR 2825276
                       A 1
                            20021206
                       Α
                            20010531
PRAI FR 2001-7149
     The invention concerns a vaccine adjuvant solid compn.
     characterized in that it comprises a solid support for injection
     and in particular a compn. further comprising a surfactant or a mixt. of
     surfactants. The invention also concerns a method for prepg. such a
     compn. and its use as adjuvant phase of a vaccine
```

compn. The invention further concerns its combination with a

solid immunity adjuvant vaccine metal cation

(adjuvants; solid form immunity adjuvant and

antigenic-phase lyophilizate and the pharmaceutical form comprising same.

TΤ Cations Surfactants Vaccines

Immunostimulants

vaccine contg. same)

ST IT

```
(solid form immunity adjuvant and vaccine contg.
        same)
    Carbohydrates, biological studies
TT
     Polysaccharides, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (solid form immunity adjuvant and vaccine contg.
        same)
     50-99-7, Dextrose, biological studies
                                             63-42-3, Lactose
                                                                 69 - 65 - 8,
IT
                                             299-28-5, Calcium gluconate
                139-12-8, Aluminum acetate
    Mannitol
                                     994-36-5,
    546-93-0, Magnesium carbonate
    Sodium citrate
                      1305-62-0, Calcium hydroxide, biological studies
    1320-46-3, Manganese glycerophosphate
                                             4468-02-4, Zinc gluconate
                                     7631-86-9, Silica, biological studies
     6485-39-8, Manganese gluconate
     9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin
                                                                      9004-57-3,
     Ethyl cellulose
                       9004-65-3, Hydroxypropyl methyl cellulose
                                                                   9004-67-5,
                        12619-70-4, Cyclodextrin
                                                   14127-61-8, Calcium cation,
    Methyl cellulose
    biological studies
                          14903-36-7, biological studies
                                                           15479-57-9, Aluminum
                  17375-37-0, Manganese carbonate
                                                    20074-52-6, Ferric cation,
                          21059-46-1, Calcium L-aspartate
                                                            22537-22-0,
    biological studies
                                           23713-49-7, Zinc cation, biological
    Magnesium cation, biological studies
               84285-67-6
                            206360-00-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (solid form immunity adjuvant and vaccine contg.
        same)
RE.CNT
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Csl Limited; WO 9415636 A 1994 HCAPLUS
(2) Eastbridge Limited; WO 9841188 A 1998 HCAPLUS
(3) Meditest; GB 1379008 A 1975 HCAPLUS
(4) Seppic; EP 1095662 A 2001 HCAPLUS
IT
     546-93-0, Magnesium carbonate
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (solid form immunity adjuvant and vaccine contg.
        same)
RN
     546-93-0 HCAPLUS
    Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
   \circ
HO-C-OH
   Mg
L89 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2003 ACS
    2002:852314 HCAPLUS
ΑN
    Controlled delivery of metoclopramide using an injectable
TΙ
     semi-solid poly(ortho ester) for veterinary application
     Schwach-Abdellaoui, Khadija; Moreau, Marinette; Schneider, Marc; Boisramc,
ΑU
     Bernard; Gurny, Robert
     School of Pharmacy, Laboratory of Pharmaceutical Technique and
CS
     Biopharmacy, University of Geneva, Geneva, CH-1211, Switz.
     International Journal of Pharmaceutics (2002), 248(1-2), 31-37
SO
    CODEN: IJPHDE; ISSN: 0378-5173
PB
    Elsevier Science B.V.
DT
    Journal
LΑ
    English
CC
     63 (Pharmaceuticals)
     In animal health care, current therapeutic regimens for gastrointestinal
AB
```

disorders require repeated oral or parenteral dosage forms of anti-emetic agents. However, fluctuations of plasma concns. produce severe side effects. The aim of this work is to develop a s.c. and biodegradable controlled release system contg. metoclopramide (MTC). Semi-solid poly(ortho ester)s (POE) prepd. by a transesterification reaction between tri-Me orthoacetate and 1,2,6,-hexanetriol were investigated as injectable bioerodible polymers for the controlled release of MTC. MTC is present in the polymeric matrix as a solubilised form and it is released rapidly from the POE by erosion and diffusion because of its acidic character and its high hydrosoly. manual injection is desired, only low mol. wt. can be used. However, low mol. wt. POEs release the drug rapidly. In order to extend polymer lifetime and decrease drug release rate, a sparingly water-sol. base Mg(OH) 2 was incorporated to the formulation. It was possible to produce low mol. wt. POE that can be manually injected and releasing MTC over a period of several days.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Beckett, A; Arzneim Forsch 1987, V37, P221 HCAPLUS
- (2) Bruera, E; Cancer 1994, V74, P3204 MEDLINE
- (3) Einmahl, S; Biomed Mater Res 2000, V50, P566 HCAPLUS
- (4) Einmahl, S; Int J Pharm 1999, V185, P189 HCAPLUS
- (5) El-Sayed, Y; Int J Pharm 1995, V123, P113 HCAPLUS
- (6) Harrison, F; Arzneim Forsch 1994, V44, P519 HCAPLUS
- (7) Heller, J; Adv Polym Sci 1993, V107, P41 HCAPLUS
- (8) Madej, T; Br J Clin Pharmacol 1988, V26, P747 MEDLINE
- (9) Merkli, A; J Biomater Sci Polym Edn 1993, V4, P505 HCAPLUS
- (10) Merkli, A; J Control Release 1994, V29, P105 HCAPLUS
- (11) Merkli, A; J Control Release 1995, V33, P415 HCAPLUS
- (12) Roskos, K; Biomaterials 1995, V16, P313 HCAPLUS
- (13) Zignani, M; J Biomed Mater Res 1998, V39, P277 HCAPLUS
- L89 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2003 ACS
- AN 2002:793349 HCAPLUS
- DN 137:293545
- TI Immunity adjuvant containing a complexed metal cation and vaccine containing same
- IN Trouve, Gerard; Dupuis, Laurent
- PA Societe d'Exploitation de Produits pour les Industries Chimiques SEPPIC, Fr.
- SO PCT Int. Appl., 23 pp. CODEN: PIXXD2
- DT Patent
- LA French
- IC ICM A61K
- CC 15-2 (Immunochemistry)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
					-
PΙ	WO 2002080840	A2	20021017	WO 2002-FR1057	20020327
	WO 2002080840	A3	20030103		

W: JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

FR 2823119 A1 20021011 FR 2001-4644 20010405 PRAI FR 2001-4644 A 20010405

AB The invention relates to a compn. comprising a fatty phase and a non-null quantity of an organometallic gel obtained by complexing an anionic polymer or a mixt. of different anionic polymers with a multivalent metal cation or a mixt. of different metal cations. Said compn. is preferably in the form of an emulsion, the continuous phase of which is the fatty

phase and the dispersed phase is the multivalent metal cation-anionic polymer gel complex. The invention also relates to the method for prepg. the emulsion consisting in: prepg. an aq. suspension contq. at least one insol. multivalent cation salt, at least one water-sol. anionic polymer and optionally at least one hydrophilic surfactant; emulsifying the suspension thus prepd., with an oil phase contq. optionally one lipophilic surfactant; if necessary, solubilizing the insol. multivalent cation salt by modifying the pH of the emulsion; optionally adding an excess of multivalent cation; and neutralizing the final emulsion obtained. invention also relates to the vaccine contq. said compn. Prepn. of an emulsion contg. calcium alginate gel as immunoadjuvant is disclosed. immunoadjuvant complex metal cation vaccine calcium alginate Immunostimulants (adjuvants; immunity adjuvant contg. complexed metal cation and vaccine contq. same) Fats and Glyceridic oils, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (animal; immunity adjuvant contg. complexed metal cation and vaccine contq. same) Polyelectrolytes (anionic, complexes with multivalent metal cations; immunity adjuvant contq. complexed metal cation and vaccine contq. same) Cations (complexes with anionic polymers; immunity adjuvant contg. complexed metal cation and vaccine contg. same) Fatty acids, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (esters; immunity adjuvant contg. complexed metal cation and vaccine contq. same) Carbohydrates, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ethers; immunity adjuvant contq. complexed metal cation and vaccine contg. same) Alcohols, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fatty, ethers with polyols; immunity adjuvant contg. complexed metal cation and vaccine contg. same) Fats and Glyceridic oils, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hazelnut; immunity adjuvant contq. complexed metal cation and vaccine contq. same) Gums and Mucilages Surfactants Vaccines (immunity adjuvant contg. complexed metal cation and vaccine contg. same) Acrylic polymers, biological studies Castor oil Coconut oil Cod liver oil Corn oil Glycerides, biological studies Hydrocarbon oils Olive oil Palm oil Paraffin oils Peanut oil Rape oil Soybean oil Sunflower oil RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(immunity adjuvant contg. complexed metal cation and

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ΙT

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vaccine contq. same)
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- IT Carboxylic acids, biological studies
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polycarboxylic; immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- IT Fats and Glyceridic oils, biological studies
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sesame; immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- IT Fats and Glyceridic oils, biological studies
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vegetable; immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- IT Fats and Glyceridic oils, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (walnut; immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- IT Fats and Glyceridic oils, biological studies
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (wheat germ; immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- IT 50-21-5, Lactic acid, reactions 64-19-7, Acetic acid, reactions
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 (immunity adjuvant contg. complexed metal cation and
 vaccine contg. same)
- 50-70-4D, Sorbitol, esters with fatty acids 50-99-7D, Glucose, ethers ΙT 57-10-3D, Palmitic acid, esters 57-50-1D, Sucrose, esters 57-55-6D, Propylene glycol, esters with fatty acids 58-86-6D, Xylose, ethers 69-65-8D, Mannitol, esters with fatty acids 110-27-0, Isopropyl 111-01-3, Squalane 111-02-4, Squalene 111-62-6, Ethyl myristate 112-62-9, Methyl oleate 112-80-1D, Oleic acid, esters oleate 141-22-0D, Ricinoleic acid, esters 139-12-8, Aluminum acetate 299-28-5, Calcium gluconate 544-63-8D, Myristic acid, esters 585-86-4D, 546-93-0, Magnesium carbonate 598-62-9, Manganese carbonate 1305-62-0, Calcium Lactitol, ethers hydroxide, biological studies 1320-46-3, Manganese glycerophosphate 1338-43-8, Montane 80 4468-02-4, Zinc gluconate 6485-39-8, Manganese gluconate 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-69-5, 9004-54-0, Dextran, biological studies 9005-32-7, Alginic acid Pectin 9005-38-3, Sodium alginate 9005-65**-**6, Montanox 80 11138-66-2, Xanthan 12441-09-7D, Sorbitan, esters 12441-09-7D, Sorbitan, esters with 14127-61-8, Calcium cation, biological studies 14127-69-6, fatty acids biological studies 14903-36-7, biological studies 15479-57-9, Aluminum salicylate 16958-85-3, Octyl palmitate 20074-52-6, Ferric ion, biological studies 22537-22-0, Magnesium cation, biological studies 23713-49-7, Zinc cation, biological studies 25618-55-7D, Polyglycerol, esters with fatty acids 30399-84-9D, Isostearic acid, esters 34828-64-3D, Mannitan, esters 34828-64-3D, Mannitan, esters with fatty 55608-27-0D, Hexol, esters with fatty acids 206360-00-1 468084-13-1, Montanide ISA 564 468084-14-2, Montanide ISA 763 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (immunity adjuvant contg. complexed metal cation and
- vaccine contg. same)
 IT 546-93-0, Magnesium carbonate
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (immunity adjuvant contg. complexed metal cation and vaccine contg. same)
- RN 546-93-0 HCAPLUS
- CN Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)

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Mg

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T.89
    ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ΑN
     2002:657929 HCAPLUS
ÐΝ
    137:206535
ΤI
    Composition and method for controlled release injections
ΤN
    Roser, Bruce
PΑ
    Cambridge Biostability Ltd., UK; Idea, Inc.
SO
     PCT Int. Appl., 23 pp.
    CODEN: PIXXD2
DT
    Patent
LΑ
    English
IC
     ICM A61K009-00
     ICS A61K009-16
CC
     63-6 (Pharmaceuticals)
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO.
                                                            DATE
                                           ______
    WO 2002066005
                            20020829
                                           WO 2002-US4269
                                                            20020214
PΙ
                     A1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                      A1
     US 2002155129
                            20021024
                                           US 2001-784153
                                                            20010216
PRAI US 2001-784153
                      Α
                            20010216
AΒ
    The present invention is a pharmaceutical compn. and method for
    controlling the release of a drug or vaccine to a patient where
    a slow, controlled release of drug or antigen occurs over a considerable
    period of time after injection. The drug or vaccine
     is contained in sugar glass microspheres and then placed in an anhyd.
    liq., preferably perfluorocarbon, so that the vaccine is
    protected against dissoln. while remaining surrounded by anhyd. liq.
     simple non-toxic system, deliverable by current syringe or present or
     future needle-free systems, is inexpensive and reliable and aids in
    parenteral drug delivery or mass immunization campaigns by
    reducing the need for repeated injections. There was a slow
     controlled-release of model antigen (alk. phosphatase) which had been
     suspended in perfluorophenanthrene.
ST
    controlled release injection perfluorocarbon
ΙT
    Analgesics
    Anti-inflammatory agents
    Anticoagulants
    Antitumor agents
     Bacteria (Eubacteria)
     Buffers
    Cardiovascular agents
    Contraceptives
     Immunomodulators
```

```
· Immunosuppressants
     Opioid antagonists
     Protozoa
       Vaccines
     Vasodilators
        (controlled release injections contg. perfluorocarbons)
     Polysiloxanes, biological studies
TΤ
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (controlled release injections contg. perfluorocarbons)
     Alditols
ΤТ
     Antigens
     Carbohydrates, biological studies
     DNA
     Glass microspheres
     Hormones, animal, biological studies
     Lipids, biological studies
     Lipoproteins
     Peptides, biological studies
     Perfluorocarbons
     Proteins
     RNA
     Toxins
     Toxoids
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (controlled release injections contg. perfluorocarbons)
TΨ
     Drug delivery systems
        (injections, sustained release;
        controlled release injections contg. perfluorocarbons)
TΤ
     Drying
        (spray; controlled release injections contg.
        perfluorocarbons)
ŦΤ
     Toxoids
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tetanus; controlled release injections contg.
        perfluorocarbons)
ΤТ
     50-70-4, Glucitol, biological studies
                                               57-50-1, Sucrose, biological
               69-65-8, D-Mannitol 77-86-1, Tris 87-89-8, Inositol
     studies
                                                                      512-69-6,
     87-99-0, Xylitol 99-20-7, Trehalose 470-55-3, Stachyose
     Raffinose 585-86-4, Lactitol 585-88-6, Maltitol 2152-56-9, Arabinitol 7646-85-7, Zinc chloride, bi
                                                             608-66-2, Galactitol
                              7646-85-7, Zinc chloride, biological studies
     7727-43-7, Barium sulfate
                                  7784-30-7, Aluminum phosphate
                                                                   7786-30-3,
     Magnesium chloride, biological studies 10103-46-5, Calcium phosphate
     13463-67-7, Titania, biological studies
                                                21645-51-2,
     Aluminum hydroxide, biological studies
                                                63213-92-3, Glucopyranosyl
                134613-11-9, Glucopyranosyl mannitol
     sorbitol
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (controlled release injections contg. perfluorocarbons)
     306-94-5, Perfluorodecalin 307-34-6, Perfluorooctane 355-42-0, Perfluorohexane 1580-20-7, Perfluorophenanthrene
TΨ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (controlled release injections contg. perfluorocarbons)
              THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Eastbridge; WO 9841118 A 1998
(2) Roser, B; US 6190701 B1 2001 HCAPLUS
(3) Universal Preservation Technologies; WO 0137804 A 2001 HCAPLUS
     13463-67-7, Titania, biological studies
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (controlled release injections contg. perfluorocarbons)
RN
     13463-67-7 HCAPLUS
```

CN Titanium oxide (TiO2) (8CI, 9CI) (CA INDEX NAME)

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O== Ti== O
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ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
ΑN
     2002:293473 HCAPLUS
DN
     136:308528
TΙ
     Vaccine compositions comprise Yershinia adhesion protein as
     adjuvant
     Hermand, Philippe; Vande Velde, Vincent
ΙN
     Smithkline Beecham Biologicals S.A., Belg.
PΑ
SO
     PCT Int. Appl., 46 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K039-39
     ICS A61P031-00; A61P033-00; A61P035-00
CC
     15-2 (Immunochemistry)
     Section cross-reference(s): 63
FAN.CNT 1
                                           APPLICATION NO.
                                                            DATE
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                      KIND DATE
     ______
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                           _____
                                           -----
                            20020418
                                           WO 2001-EP3786
                                                            20010326
PΙ
     WO 2002030458
                      Α1
     WO 2002030458
                      C1
                            20020718
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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     AU 2001062163
                     Α5
                            20020422
                                         AU 2001-62163
                                                            20010326
PRAI GB 2000-25058
                       Α
                            20001012
     WO 2001-EP3786
                       W
                            20010326
ΑB
     The present invention relates to adjuvant compns. which are
     suitable to be used in vaccines. In particular, the
     adjuvant compns. of the present invention comprises a Yersinia
     adhesion protein, optionally with a carrier. Also provided by the present
     invention are vaccines comprising the adjuvants of the
     present invention and an antigen. Further provided are methods of manuf.
     of the adjuvants and vaccines of the present invention
     and their use as medicaments. Methods of treating an individual
     susceptible to or suffering from a disease by the administration of the
     vaccines of the present invention are also provided.
ST
     Yershinia adhesion protein adjuvant vaccine carrier
TΤ
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (17-1A; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
ΙT
     Oligonucleotides
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (CpG-contg.; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
ΙT
     Proteins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (PAP (pokeweed antiviral protein); vaccine compns. comprise
```

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Yershinia adhesion protein as adjuvant)
    Antigens
ΙT
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (PSMA or prostate-specific membrane antigen; vaccine compns.
        comprise Yershinia adhesion protein as adjuvant)
TΤ
    Proteins
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (adhesive; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
     Immunostimulants
        (adjuvants; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
TT
    Gene, microbial
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (ail; vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
ΙΤ
    Infection
        (bacterial; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
IT
    Spheres
        (beads, latex; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
    Latex
        (beads; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
TΤ
    Drug delivery systems
        (buccal; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
    Drug delivery systems
IT
        (carriers; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
    Peptides, biological studies
ΙT
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (decapeptides, Stanworth; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
IT
    Drug delivery systems
        (diluent and excipient; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
    Escherichia coli
IT
        (enterotoxigenic; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
     Polyoxyalkylenes, biological studies
ΙT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ethers and esters; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
ΙT
    Mucins
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (gene MUC1; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
IT
    Lipoproteins
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (gene ospA, lipided; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
ΙT
     Parasite
        (infection; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
ΙT
     Drug delivery systems
        (intraduodenal; vaccine compns. comprise Yershinia adhesion
```

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protein as adjuvant)
    Gene, microbial
ΙT
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (inv; vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
TT
    Proteins
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (invasins; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
    Antigens
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (melanoma-assocd., BAGE; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
    Antigens
IT
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (melanoma-assocd., GAGE; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
    Antigens
TΨ
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (melanoma-assocd., MAGE; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
TΤ
    Animal virus
        (meningitis; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
    Particles
        (metallic salt; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
    Drug delivery systems
        (mucosal, vaccine; vaccine compns. comprise
        Yershinia adhesion protein as adjuvant)
TΤ
    Drug delivery systems
        (nasal, intra-; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
ΙT
    Salts, biological studies
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (particle; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
    Polymers, biological studies
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (porous particle; vaccine compns. comprise Yershinia adhesion
       protein as adjuvant)
ΙT
    Cell adhesion molecules
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (protein; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
ΙT
    Toxoids
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (tetanus; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
IT
    Antigens
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (tumor-assocd., PRAME; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
ΙT
    Antigens
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
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(Biological study); USES (Uses)
        (tumor-assocd.; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
ΙT
    Vaccines
        (tumor; vaccine compns. comprise Yershinia adhesion
        protein as adjuvant)
ΙT
     Haemophilus influenzae
        (type b; vaccine compns. comprise Yershinia adhesion protein
        as adjuvant)
ΙT
    Allergy
     Antitumor agents
     Bordetella
     Borrelia
     Borrelia burgdorferi
     Campylobacter
     Chlamydia
     Dengue virus
     Haemophilus
     Hepatitis A virus
     Hepatitis B virus
     Hepatitis C virus
     Hepatitis E virus
     Human herpesvirus 1
     Human herpesvirus 2
     Human herpesvirus 3
     Human herpesvirus 5
     Human immunodeficiency virus
     Human papillomavirus
     Immunostimulants
     Infection
     Influenza virus
    Mammalia
    Microspheres
    Moraxella
    Mycobacterium
    Mycoplasma
    Nanoparticles
     Neisseria
     Pathogen
     Plasmodium (malarial genus)
     Respiratory syncytial virus
     Salmonella
     Streptococcus
     Susceptibility (genetic)
     Toxoplasma
     Yersinia
     Yersinia enterocolitica
     Yersinia pseudotuberculosis
        (vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
    Antigens
     Carcinoembryonic antigen
     Prostate-specific antigen
     neu (receptor)
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
ΙT
    Antitumor agents
        (vaccines; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
ΙT
     Infection
        (viral; vaccine compns. comprise Yershinia adhesion protein
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as adjuvant)
TΤ
     2382-65-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (oligonucleotides contg.; vaccine compns. comprise Yershinia
        adhesion protein as adjuvant)
     9034-40-6, Luteinizing hormone-releasing hormone
                                                        137632-09-8, Her-2
IT
     kinase
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
     471-34-1, Calcium carbonate, biological studies 546-93-0,
TT
     Magnesium carbonate 1309-42-8,
                           7000-29-5, Calcium
     Magnesium hydroxide
                           7757-87-1
                                      7758-87-4, Calcium
     magnesium carbonate
                 7778-18-9, Calcium sulfate 7784-30-7, Aluminum phosphate
     phosphate
     9002-10-2, Tyrosinase 10045-86-0, Iron phosphate
                                                         15905-72-3, Calcium
                      21645-51-2, Aluminum hydroxide, biological studies
     iron phosphate
                                      35918-42-4, Iron potassium phosphate
     25322-68-3D, ethers and esters
     52767-99-4, Ammonium iron phosphate
                                           128478-31-9, 3D-MPL
                         226408-87-3, Prostase
     141256-04-4, QS 21
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
RE.CNT
              THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Falkow, S; US 5239066 A 1993 HCAPLUS
(2) Falkow, S; US 5338842 A 1994 HCAPLUS
(3) Oaks; ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR
    MICROBIOLOGY 1999, V99, P282
(4) Oaks, E; WO 0018354 A 2000 HCAPLUS
(5) Picking, W; WO 0023462 A 2000 HCAPLUS
IT
     546-93-0, Magnesium carbonate
     1309-42-8, Magnesium hydroxide
     141256-04-4, QS 21
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vaccine compns. comprise Yershinia adhesion protein as
        adjuvant)
RN
     546-93-0 HCAPLUS
CN
     Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
   0
но-с-он
    Mq
RN
     1309-42-8 HCAPLUS
     Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
CN
HO-Mq-OH
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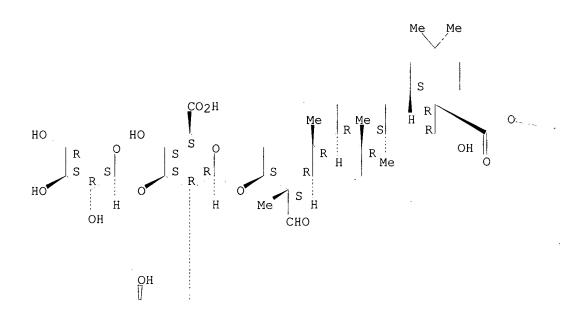
141256-04-4 HCAPLUS .beta.-D-Glucopyranosiduronic acid, (3.beta.,4.alpha.,16.alpha.)-28-[[O-D-CN apio-.beta.-D-furanosyl-(1.fwdarw.3)-O-.beta.-D-xylopyranosyl-(1.fwdarw.4)-arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-

RN

1-oxooctyl]-6-deoxy-.beta.-D-galactopyranosyl]oxy]-16-hydroxy-23,28-dioxoolean-12-en-3-yl O-.beta.-D-galactopyranosyl-(1.fwdarw.2)-O-[.beta.-D-xylopyranosyl-(1.fwdarw.3)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-C

PAGE 2-A

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HO R S O HO

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L89 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2003 ACS
    2002:142547 HCAPLUS
ΑN
    136:189316
DN
TI
    Oral solid dose vaccine
IN
    Vande-Velde, Vincent
PΑ
    Smithkline Beecham Biologicals S.A., Belg.
SO
    PCT Int. Appl., 32 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
    A61K039-39; A61K039-00; A61K009-20; A61K039-02; A61K039-12
IC
CC
    63-3 (Pharmaceuticals)
FAN.CNT 1
                     KIND DATE
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                    A1 20020221
    WO 2002013858
                                       WO 2001-IB1711 20010814
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            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2001086168
                    A5 20020225
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                                                         20010814
                    . A
PRAI GB 2000-20089
                           20000815
                    W
                           20010814
    WO 2001-IB1711
AB
    The present invention relates to novel vaccine formulations
    suitable for oral administration. The vaccine formulations are
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in a solid form comprising antigen and suitable excipient, which after

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insertion into the mouth, rapidly dissolve in saliva, thereby releasing
    the vaccine into the mouth. Specifically, the solid form may
    consist of a cake of vaccine which is formed from a liq. soln.
    or suspension by sublimation, preferably sublimation by lyophilization.
     Preferred vaccines are those contg. antigens which are derived
     from pathogens that normally infect or invade the host through a mucosal
    membrane, or those vaccines that further comprises an antacid.
     Particularly preferred vaccines are combination vaccines
     that comprise more than one antigen, and more preferably when the antigens
     are from more than one pathogen. Lyophilized oral vaccines were
    prepd. contg. influenza antigens 30 .mu.g, sucrose 2, sorbitol 3, dextran
    T40 4, amino acids 2, xanthane 0.3% and calcium carbonate 80 mg.
ST
    oral solid vaccine lyophilization
ΙT
    Hepatitis
        (C, antigens; oral solid dose vaccine contg.)
TΤ
     Immunostimulants
        (adjuvants; oral solid dose vaccine contq.)
IT
    Bordetella
    Borrelia
    Chlamydia
    Cytomegalovirus
     Dengue virus
     Human herpesvirus 1
     Human herpesvirus 2
    Human herpesvirus 3
    Human immunodeficiency virus
    Human papillomavirus
     Influenza virus
    Meningitis
    Neisseria
    Plasmodium (malarial genus)
    Respiratory syncytial virus
    Salmonella
    Toxoplasma
        (antigens; oral solid dose vaccine contg.)
    Peptides, biological studies
TΤ
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (decapeptides, stanworth; oral solid dose vaccine contg.)
    Antigens
IT
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (hepatitis A; oral solid dose vaccine contg.)
TΤ
    Antigens
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (hepatitis B; oral solid dose vaccine contg.)
TT
    Antacids
    Stabilizing agents
    Thixotropic agents
        (oral solid dose vaccine contg.)
ΙT
    Alditols
    Antigens
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (oral solid dose vaccine contg.)
IT
    Vaccines
        (oral; oral solid dose vaccine)
    Alcohols, biological studies
IT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (polyhydric; oral solid dose vaccine contg.)
IT
    Antigens
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
          (tumor-assocd.; oral solid dose vaccine contg.)
TΤ
      50-99-7, Dextrose, biological studies 57-48-7, Fructose, biological
     studies 57-50-1, Sucrose, biological studies 59-23-4, Galactose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 99-20-7, Trehalose 471-34-1, Calcium carbonate, biological
                99-20-7, Trehalose
      studies 546-93-0, Magnesium carbonate
      585-86-4, Lactitol 3458-28-4, Mannose 4618-18-2, Lactulose 9004-54-0, Dextran, biological studies 11138-66-2, Xanthan gum
      13718-94-0, Isomaltulose
                                      17606-72-3, Maltulose 21645-51-2, Aluminum
      hydroxide, biological studies
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (oral solid dose vaccine contg.)
                THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Denamur, F; WO 0112797 A 2001 HCAPLUS
(2) Seager, H; GB 1548022 A 1979 HCAPLUS
(3) Seager, H; WO 9921579 A 1999 HCAPLUS
(4) Seager, H; JOURNAL OF PHARMACY AND PHARMACOLOGY 1998, V50(4), P375 HCAPLUS
      546-93-0, Magnesium carbonate
TΤ
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
          (oral solid dose vaccine contg.)
RN
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      Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
    0
HO-C-OH
    Mq
L89 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ΑN
      2002:122817 HCAPLUS
      136:189313
DN
      Parenteral vaccine formulations containing
ΤI
      adjuvant salts
      Soni, Nanna Kristensen; Rahbek, Janne Uldal;
TN
      Aasmul-Olsen, Stig; Lund, Lise
PΑ
     Alk-Abello A/S, Den.
SO
      PCT Int. Appl., 59 pp.
      CODEN: PIXXD2
DT
      Patent
LA
      English
IC
      ICM A61K039-39
      ICS A61P037-04
CC
      63-3 (Pharmaceuticals)
      Section cross-reference(s): 15
FAN.CNT 1
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                                                 WO 2001-DK532 20010809 <--
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                         A1 20020214
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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                                           AU 2001-79601
     AU 2001079601
                       Α5
                            20020218
                                                             20010809 <--
     US 2002051794
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                                            US 2001-925635
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PRAI DK 2000-1194
                       Α
                            20000809
                                      <--
     US 2000-224037P
                       Ρ
                            20000809
     WO 2001-DK532
                       W
                            20010809
AB
     A parenteral vaccine formulation comprises at least
     one immunogenic substance, and as an adjuvant, one or more salts
     of Group 2 or Group 4 elements and their hydrates. When the
     adjuvant salt is included in parenteral vaccine
     formulations, the amt. of antigen necessary to induce an immune response,
     following one immunization, is reduced. The vaccines contg.
     adjuvant salts induced a persistent and specific immune response.
     Furthermore, an earlier onset is obsd., and the magnitude of the immune
     response is comparable to that seen with vaccine formulations
     contg. aluminum hydroxide as an adjuvant.
ST
     salt immunol adjuvant parenteral vaccine
TΤ
     Saponins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (MPL; parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
TΤ
     Immunostimulants
        (adjuvants; parenteral vaccine
        formulations contg. adjuvant salts and their hydrates)
ΙT
     Phosphates, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (hydrogen; parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
     Polyesters, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (hydroxycarboxylic acid-based; parenteral vaccine
        formulations contg. adjuvant salts and their hydrates)
TΨ
     Drug delivery systems
        (injections, epicutaneous; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
ΙT
     Drug delivery systems
        (injections, i.m.; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
TT
     Drug delivery systems
        (injections, i.p.; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
TT
     Drug delivery systems
        (injections, i.v.; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
ΙT
     Drug delivery systems
        (injections, intra-articular; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
IT
     Drug delivery systems
        (injections, intradermal; parenteral
        vaccine formulations contg. adjuvant salts and their
        hydrates)
IT
     Drug delivery systems
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(injections, s.c.; parenteral

```
vaccine formulations contg. adjuvant salts and their
        hydrates)
ΙT
     Salts, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (org.; parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
IT
     Buffers
    Coloring materials
    Dispersing agents
    `Human
    Solubilizers
    Vertebrata
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
TI
    Carbonates, reactions
    Peroxides, reactions
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
TΤ
    Hydroxides (inorganic)
    Oxides (inorganic), biological studies
     RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
     (Reactant or reagent); USES (Uses)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
ΙΤ
    Antigens
     Diphosphates
    Lecithins
     Phosphates, biological studies
     Polyolefins
     Salts, biological studies
     Saponins
     Silicates, biological studies
     Sulfates, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
ΙT
    Vaccines
        (parenteral; parenteral vaccine
        formulations contg. adjuvant salts and their hydrates)
IT
    Alkaline earth metals
    Group IVB elements
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (salts; parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
ΙT
    Toxoids
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tetanus; parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
     144-55-8, Sodium hydrogen carbonate, biological studies
                                                                7647-14-5,
ΤТ
     Sodium chloride, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (buffer contg.; parenteral vaccine formulations
        contg. adjuvant salts and their hydrates)
                                       7440-32-6, Titanium, reactions
TT
     7439-95-4, Magnesium, reactions
                                    7440-67-7, Zirconium, reactions
     7440-39-3, Barium, reactions
     7440-70-2, Calcium, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
     471-34-1, Calcium carbonate, biological studies
                                                        513-77-9, Barium
ΙT
     carbonate 546-93-0, Magnesium carbonate
                                  1304-56-9, Beryllium oxide, biological
     1304-29-6, Barium peroxide
```

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1305-62-0, Calcium hydroxide, biological studies
                                                                  1305-79-9,
     Calcium peroxide 1309-42-8, Magnesium
                1309-48-4, Magnesium oxide, biological studies
     hydroxide
     1314-18-7, Strontium peroxide 1314-23-4, Zirconium dioxide, biological
               1343-88-0, Magnesium silicate
                                              1344-28-1, Aluminum oxide,
     biological studies 1633-05-2, Strontium carbonate 7429-90-5D,
                      7439-95-4D, Magnesium, salts
                                                      7440-14-4D, Radium, salts
     Aluminum, salts
     7440-24-6D, Strontium, salts
                                   7440-32-6D, Titanium, salts
                                                                  7440-39-3D,
                     7440-58-6D, Hafnium, salts
                                                  7440-67-7D, Zirconium, salts
     Barium, salts
     7440-70-2D, Calcium, salts 7487-88-9, Magnesium sulfate, biological
               7727-43-7, Barium sulfate 7757-87-1, Trimagnesium phosphate
     7757-93-9, Calcium hydrogen phosphate 7758-23-8, Calcium dihydrogen
                 7758-87-4, Tricalcium phosphate 7778-18-9, Calcium sulfate
     phosphate
     7790-76-3, Calcium pyrophosphate 10034-77-2, Dicalcium silicate
                10101-41-4, Calcium sulfate dihydrate 10 12168-85-3, Tricalcium silicate 13463-67-7,
     10101-39-0
                                                          10103-46-5, Calcium
                                            13693-11-3,
     Titanium dioxide, biological studies
     Titanium disulfate 14066-20-7, Dihydrogen phosphate, biological studies
     14452-57-4, Magnesium dioxide 14475-63-9, Zirconium hydroxide
     14644-61-2, Zirconium sulfate 14987-04-3, Magnesium trisilicate
     17194-00-2, Barium hydroxide 20427-58-1, Zinc hydroxide
                                                                 21645-51-2,
     Aluminum hydroxide, biological studies 26780-50-7, Poly
     (lactide-co-glycolide) 34346-01-5,
     Glycolic acid-lactic acid copolymer
     53850-36-5D, Rutherfordium, salts 56378-72-4 66594-14-7,
     Quil A 141256-04-4, Qs-21
     172889-84-8, MF59
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RF.
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ΙT
     546-93-0, Magnesium carbonate
     1309-42-8, Magnesium hydroxide
     13463-67-7, Titanium dioxide, biological
     studies 26780-50-7, Poly(lactide-co
     -glycolide) 34346-01-5, Glycolic
     acid-lactic acid copolymer 66594-14-7
     , Quil A 141256-04-4, Qs-
     21 172889-84-8, MF59
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (parenteral vaccine formulations contg.
        adjuvant salts and their hydrates)
RN
     546-93-0 HCAPLUS
     Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
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О || но- с- он

Mg

CN Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)

 ${\rm HO-Mg-OH}$

RN 13463-67-7 HCAPLUS

CN Titanium oxide (TiO2) (8CI, 9CI) (CA INDEX NAME)

O== Ti== O

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

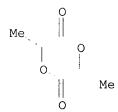
CM 1

CRN 502-97-6 CMF C4 H4 O4

0 0 0

CM 2

CRN 95-96-5 CMF C6 H8 O4



RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1 CMF C2 H4 O3

CM 2

CRN 50-21-5 CMF C3 H6 O3

RN 66594-14-7 HCAPLUS

CN Quil-A (9CI) (CA INDEX NAME)

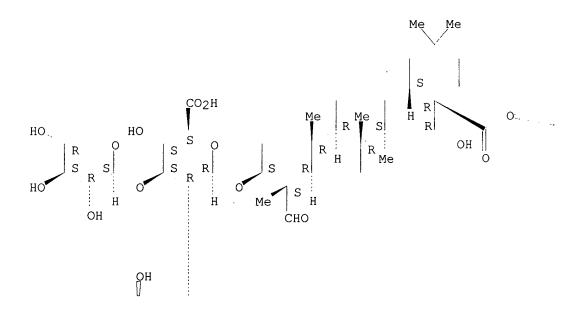
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 141256-04-4 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (3.beta.,4.alpha.,16.alpha.)-28-[[O-D-apio-.beta.-D-furanosyl-(1.fwdarw.3)-O-.beta.-D-xylopyranosyl-(1.fwdarw.4)-O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.2)-4-O-[5-[[5-(.alpha.-L-arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-1-oxooctyl]-6-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.2)-O-[.beta.-D-xylopyranosyl-(1.fwdarw.3)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

PAGE 1-C

ОН

HO. R S O HO. HO.

PAGE 2-A

RN 172889-84-8 HCAPLUS

CN Sorbitan, tri-(92)-9-octadecenoate, mixt. with (2E,6E,10E,14E,18E,22E)-2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene and sorbitan mono-(9Z)-9-octadecenoate poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

CM 1

CRN 9005-65-6

CMF Unspecified CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 111-02-4 CMF C30 H50

Double bond geometry as shown.

PAGE 1-A Ме Ме E Ε Me₂C E Ε Ме Ме

PAGE 1-B

CMe₂

CM3

CRN 1333-71-7 CMF C60 H110 O9

CCI IDS

CM

112-80-1 CRN CMF C18 H34 O2

Double bond geometry as shown.

$$(CH_2)_7$$
 Z $(CH_2)_7$ Me

CM 5

CRN 50-70-4 CMF C6 H14 O6

Absolute stereochemistry.

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ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
     2001:792223 HCAPLUS
ΑÑ
     135:348878
DN
     Therapeutic treatment and prevention of infections with a bioactive
ΤI
     materials encapsulated within a biodegradable-biocompatible polymeric
     matrix
     Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot;
IN
     Jeyanthi, Ramasubbu; Boedeker, Edgar C.; Mcqueen, Charles E.; Jarboe,
     Daniel L.; Cassels, Frederick; Brown, William; Thies, Curt; Tice, Thomas
     R.; Roberts, F. Donald; Friden, Phil
     United States of America as Represented by the Secretary of the Army, USA
PA
     U.S., 141 pp., Cont.-in-part of U.S. Ser. No. 590,973, abandoned.
SO
     CODEN: USXXAM
DT
     Patent
LA
     English
     A61K009-52; A61K047-30
IC
NCL
     424486000
     63-6 (Pharmaceuticals)
CC
     Section cross-reference(s): 1
FAN.CNT 12
                      KIND DATE
                                           APPLICATION NO.
                                                            DATE
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     US 6309669
                            20011030
                                           US 1997-789734
                                                            19970127
PΙ
                      В1
                                           US 1992-867301
     US 5417986
                      Α
                            19950523
                                                            19920410
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                                           US 1995-446148
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     WO 9832427
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             UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             GA, GN, ML, MR, NE, SN, TD, TG
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                       A1
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     WO 1998-US1556
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                            19980127
     Novel burst-free, sustained-release biocompatible and biodegradable
AB
     microcapsules which can be programmed to release their active core for
     variable durations ranging from 1-100 days in an aq. physiol. environment
     are disclosed. The microcapsules are comprised of a core of polypeptide
     or other biol. active agent encapsulated in a matrix of poly(
     lactide/glycolide) copolymer, which may
     contain a pharmaceutically-acceptable adjuvant, as a blend of
     upcapped free carboxyl end group and end-capped forms ranging in ratios
```

from 100/0 to 1/99. Ampicillin microcapsules effectively prevented infection in 73% of rats whose wound were inoculated with ampicillin-resistant strains of Staphilococcus aureus, while systemic ampicillin failed in 100% of animals.

ST bioactive microcapsule biodegradable biocompatible polymer; ampicillin microcapsule polylactide polyglycolide

IT Antitumor agents

(Kaposi's sarcoma; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Immunostimulants

(adjuvants; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Rauvolfia

(alkaloid; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Glycosides

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Drugs

(appetite stimulants; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Natural products, pharmaceutical

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (belladonna; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biodegradable; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(capsules; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Vasodilators

(coronary; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Alkaloids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ergot; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Amino acids, biological studies

Fats and Glyceridic oils, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (essential; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Fatty acids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (esters; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Embryo, animal

(fetus; therapeutic treatment and prevention of infections with

bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Calymmatobacterium granulomatis

(granuloma inguinale from; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Human herpesvirus 3

(herpes zoster from; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Fertility

(inhibitors, non-steroidal; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Disease, animal

(lymphopathia venerum; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Antibiotics

(macrolide; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(microcapsules; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Surfactants

(nonionic; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Anti-inflammatory agents

(nonsteroidal; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Nitrites

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (org.; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(prodrugs; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Alkaloids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (quinolone, fluoro-; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Antitumor agents

(sarcoma; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(solns.; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Muscle relaxants

(spasmolytics; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Contraceptives

(spermicidal; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible

polymeric matrix) Appetite ΤТ (stimulants; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix) ΙT Absidia ramosa Actinobacillus equuli Actinobacillus seminis Adrenoceptor agonists Allergy inhibitors Analgesics Anesthetics Anti-inflammatory agents Antiarrhythmics Antibacterial agents Antibiotics Anticoaqulants Anticonvulsants Antidepressants Antiemetics Antihistamines Antihypertensives Antimalarials Antimigraine agents Antiparkinsonian agents Antipyretics Antitumor agents Antitussives Antiviral agents Appetite depressants Arcanobacterium pyogenes Aspergillus fumigatus Babesia caballi Bile Blood plasma Bovine herpesvirus 1 Bronchodilators Brucella melitensis Campylobacter fetus Campylobacter fetus intestinalis Candida albicans Candida tropicalis Cardiotonics Cardiovascular agents Cardiovascular system Chlamydia psittaci Cholinergic agonists Clostridium tetani Contraceptives Cytotoxic agents Decongestants Digesters Diuretics Electrolytes Encapsulation Equid herpesvirus 1 Equine arteritis virus Escherichia coli Expectorants Fungicides

Gardnerella vaginalis Haemophilus ducreyi Human herpesvirus 1

Human herpesvirus 2 Hypnotics and Sedatives Immunomodulators Leptospira interrogans pomona Listeria monocytogenes Microorganism Muscle relaxants Mycobacterium tuberculosis Mycoplasma bovigenitalium Mycoplasma hominis Narcotics Neisseria gonorrhoeae Nutrients Opioid antagonists Parasiticides Pseudomonas aeruginosa Psychotropics Rhodococcus equi Salmonella abortus Salmonella abortusovis Stabilizing agents Streptocarpus Surfactants Toxoplasma gondii Tranquilizers Treponema pallidum Trichomonas vaginalis Tritrichomonas foetus Trypanosoma equiperdum Vaccines Vasodilators Wound healing (therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix) Alkaloids, biological studies Amino acids, biological studies Antibodies Antigens Carbohydrates, biological studies Enzymes, biological studies Estrogens Fatty acids, biological studies Glycolipids Glycols, biological studies Glycopeptides Glycoproteins, general, biological studies Growth factors, animal Hormones, animal, biological studies Lipids, biological studies Lipopolysaccharides Peptides, biological studies Pheromones, animal Polysaccharides, biological studies Progestogens Prostaglandins Proteins, general, biological studies Steroids, biological studies Sulfonamides Tetracyclines Vitamins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

IT

(therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT Lactams

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.beta.-; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)

IT 9001-92-7, Protease

- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inhibitors; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)
- IT 9001-54-1, Hyaluronidase 9001-60-9, Lactic dehydrogenase
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sperm; therapeutic treatment and prevention of infections with bioactive materials encapsulated within biodegradable-biocompatible polymeric matrix)
- IT50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, 50-28-2, .beta.-Estradiol, biological studies 50 - 33 - 9, Prednisolone Phenylbutazone, biological studies 50-52-2, Thioridazine 50-55-5, 50-78-2, Aspirin 51-55-8, Atropine, biological studies 52-24-4, Thiotepa 52-76-6, Lynestrenol 53-03-2, Prednisone Estrone, biological studies 53-86-1, Indomethacin 54-11-5, Nicotine; 55-48-1, Atropine sulfate 55-63-0, Nitroglycerin 55-86-7, Nitrogen 56-53-1, Diethyl stilbestrol 56-75-7, Chloramphenicol 57-27-2, Morphine, biological studies 57-33-0, Sodium pentobarbital 57-42-1, Meperidine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-85-2, Testosterone propionate 57-92-1, Streptomycin A, biological studies 58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine 58-22-0, Testosterone 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-73-1, Diphenhydramine 59-01-8, Kanamycin A 59-05-2, Methotrexate 59-92-7, L-Dopa, biological studies 61-33-6, Penicillin G, biological 67-20-9, Nitro-furantoin 68-22-4, Norethindrone Norethynodrel 69-53-4, Ampicillin 69-72-7D, Salicylic acid, derivs. 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 76-57-3, 78-11-5, Pentaerythritol tetranitrate 79-57-2, Oxytetracycline 79-64-1, Dimethisterone 91-81-6, Tripelennamine 103-90-2, Acetaminophen 113-15-5, Ergotamine 114-07-8, Erythromycin 114-49-8, Hyoscine hydrobromide 121-54-0, Benzethonium chloride 122-09-8, 125-29-1, Dihydrocodeinone 125-71-3, Dextromethorphan Phentermine 127-48-0, Trimethadione 128-62-1, Noscapine 145-94-8, Chlorindanol 155-41-9, Methscopolamine bromide 288-32-4D, Imidazole, derivs. 297-76-7, Ethynodiol diacetate 302-22-7, Chlormadinone acetate 305-03-3, Chlorambucil 309-43-3, Sodium secobarbital 315-30-0, 434-03-7, Ethisterone 439-14-5, Diazepam Allopurinol 443-48-1, Metronidazole 469-62-5 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 523-87-5, Dimenhydrinate 546-93-0, Magnesium carbonate 578-66-5D, 8 Aminoquinoline, derivs. 578-68-7D, 4-Aminoquinoline, derivs. Megestrol acetate 738-70-5, Trimethoprim 846-50-4, Temazepam 1397-89-3, Amphotericin-B 1397-94-0, Antimycin A 1403-66-3, Gentamicin 1404-26-8, Polymyxin-B; 1404-90-6, Vancomycin 1406-05-9, Penicillin 4696-76-8, Kanamycin B 5588-33-0, Mesoridazine 5633-18-1, Melengestrol 5786-21-0, Clozapine 5800-19-1, Metiapine 6533-00-2, Norgestrel 7447-40-7, Potassium chloride, biological studies 8063-07-8, Kanamycin 9000-83-3, Adenosine triphosphatase 9000-92-4, Amylase 9001-46-1, 9001-78-9 Glutamic acid dehydrogenase 9001-67-6, Neuraminidase 9001-99-4, RNase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies 9005-63-4D, Polyoxyethylene 9016-45-9, Polyethylene glycol nonylphenyl sorbitan, fatty acid esters 9035-74-9, Glycogen phosphorylase 10118-90-8, Minocycline

14271-04-6

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13292-46-1, Rifampin
     11111-12-9, Cephalosporins
     14271-05-7
                  21645-51-2, Aluminum hydroxide, biological studies
     22232-71-9, Mazindol
                            24730-10-7, Dihydroergocristine methanesulfonate
     25953-19-9, Cefazoline 26780-50-7, Poly(
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                                                         37517-28-5, Amikacin
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     32986-56-4, Tobramycin
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                                                            55268-75-2,
     53678-77-6, Muramyl dipeptide
                  61036-62-2, Teicoplanin
                                           64221-86-9, Imipenem
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                                           81103-11-9, Clarithromycin
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     82009-34-5, Cilastatin
                            82419-36-1, Ofloxacin
                                                    85721-33-1, Ciprofloxacin
                            189200-69-9, Polygen
     123781-17-9, Histatin
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (therapeutic treatment and prevention of infections with bioactive
        materials encapsulated within biodegradable-biocompatible polymeric
        matrix)
RE.CNT
              THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
       19
(1) Anon; EP 052510 B2 1994 HCAPLUS
(2) Anon; Materials 1996, P351
(3) Bodmer; US 5538739 1996 HCAPLUS
(4) Bodmer; US 5639480 1997 HCAPLUS
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(7) Damani; US 5198220 1993 HCAPLUS
(8) Dunn; US 5707647 1998
(9) Dunn; US 5990194 1999 HCAPLUS
(10) Gardner; US 4637905 1987 HCAPLUS
(11) Gombotz; US 5942253 1999 HCAPLUS
(12) Hunter; US 5716981 1998 HCAPLUS
(13) Hunter; US 5886026 1999 HCAPLUS
(14) Hunter; US 5994341 1999 HCAPLUS
(15) Jeyanthi; Proceedings International Symposium on Controlled Release of
    Bioactive
(16) Kent; US 4675189 1987 HCAPLUS
(17) Wang; J of Controlled Release 1991, V17, P23 HCAPLUS
(18) Yan; J of Con Rel 1994, V32(3), P231 HCAPLUS
(19) Yeh; A Novel Emulsification-Solvent extraction Technique for Production of
    Protein Loaded Biodegradable Microparticles for vaccine and Drug Delivery
    1995, V33(3), P437 HCAPLUS
     546-93-0, Magnesium carbonate
     26780-50-7, Poly(lactide-co-
     glycolide)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (therapeutic treatment and prevention of infections with bioactive
        materials encapsulated within biodegradable-biocompatible polymeric
        matrix)
RN
     546-93-0 HCAPLUS
     Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
HO-C-OH
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Mg

RN 26780-50-7 HCAPLUS 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione CN (9CI) (CA INDEX NAME)

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     ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
ΑN
     2001:780648 HCAPLUS
DN
     135:335147
ΤI
     Polymer-based injectable sustained release pharmaceutical
     compositions for peptide and protein drugs
ΙN
     Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim, Sang-beom; Lee, Ji-suk;
     Choi, Ho-il; Chang, Seung-gu
PΑ
     Peptron Inc., S. Korea
SO
     PCT Int. Appl., 37 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
     ICM A61K009-22
IC
     63-6 (Pharmaceuticals)
CC
FAN.CNT 1
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                                DATE
                                                  APPLICATION NO.
                                                                      DATE
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PΙ
     WO 2001078687
                         A1
                                20011025
                                                  WO 2001-KR462
                                                                      20010322
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               CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
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          RW: GH, GM,
                        ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
               DE, DK,
               BJ, CF,
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     EP 1187602
                          Α1
                                20020320
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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                                20030206
                                                  US 2002-18870
                                                                      20020418
     US 2003026844
                          A1
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PRAI KR 2000-20484

KR 2000-49344

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Α

20000418

20000824

20010322 WO 2001-KR462 Controlled and sustained release injectable pharmaceutical AB compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. biodegradable porous microspheres having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and freeze-drying the biopharmaceutical-incorporated microspheres. For example, microspheres were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened microspheres were collected by centrifugation and washed twice with 200 mL of deionized water, and then freeze-dried. The microspheres obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the microspheres into a buffer soln. having an appropriate concn. of protein. ST peptide protein polymer encapsulation controlled release microsphere; sustained release microsphere peptide protein injection Proteins, specific or class TΤ RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (A; prepn. of polymer-based injectable sustained-release. microspheres for peptide and protein drugs) IT Proteins, specific or class RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (C-reactive; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) Proteins, specific or class ΙT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (C; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) Apolipoproteins TT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (E; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) IT Acids, biological studies RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (acidifying agents; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) IT Alkali metal hydroxides RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (alkalizing agents; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) TT Quaternary ammonium compounds, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (alkylbenzyldimethyl, chlorides; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs)

IT

Functional groups Surfactants

```
(anionic; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
    Antibodies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anti-infective; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
TΤ
    Vaccines
        (antigens; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
     Polymers, biological studies
ΙT
     Polyurethanes, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (biodegradable; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
     Polyesters, biological studies
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (caprolactone-based; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
    Growth factors, animal
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (cartilage-inducing factor; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
    Surfactants
        (cationic; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
IΤ
    Glycoproteins, specific or class
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (cytotoxic; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
     Polyesters, biological studies
TT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (dilactone-based; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
    Lymphokines
TT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (erythroid-potentiating factors; prepn. of polymer-based
        injectable sustained-release microspheres for peptide and
        protein drugs)
IT
     B cell (lymphocyte)
     T cell (lymphocyte)
        (factors regulating; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
TT
     Polyesters, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (glycolide-based; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
IT
     Peptides, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immunotherapeutic; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
     Drug delivery systems
        (immunotoxins; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
    Drug delivery systems
        (injections, controlled release; prepn. of polymer-based
        injectable sustained-release microspheres for peptide and
        protein drugs)
IT
    Drug delivery systems
        (injections, sustained release; prepn. of
        polymer-based injectable sustained-release microspheres for
        peptide and protein drugs)
ΙT
     Polyesters, biological studies
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lactide; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Annexins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipomodulin; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) TT Casting process (low temp.; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) TT Cytokines RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (macrophage-activating factor; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) IT Encapsulation (microencapsulation; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) IT Drug delivery systems (microspheres, controlled-release; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Polyethers, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ortho ester group-contg.; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Growth factors, animal RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (osteogenic growth factors; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) TT Macrophage (peptides; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Functional groups (phosphoryl group; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Polyamides, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (poly(amino acids); prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) Polyesters, biological studies IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyamide-; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) Polyamides, biological studies IT Polyethers, biological studies Polyoxyalkylenes, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyester-; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Polyesters, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyether-; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Polyesters, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyoxyalkylene-; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs) ΙT Anti-infective agents Antibacterial agents Antiviral agents Carboxyl group Cryoprotectants Evaporation

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Fibrinolytics
     Freeze drying
     Particle size
     Phase separation
     Pulmonary surfactant
    Solvent extraction
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
ΙT
    Albumins, biological studies
    Fibrins
    Gelatins, biological studies
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
TΤ
    Annexins
    Bone morphogenetic proteins
    Caseins, biological studies
    Collagens, biological studies
     Fibrinogens
    Hemoglobins
    Interferons
    Interleukin 1
    Interleukins
    Lymphotoxin
    Ovalbumin
    Platelet-derived growth factors
    Polyanhydrides
    Polycarbonates, biological studies
     Polymer blends
    Polysaccharides, biological studies
    Proteins, general, biological studies
    Transferrins
    Transforming growth factors
    Tumor necrosis factors
    Zeins
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
ΙΤ
    Drying
        (spray; prepn. of polymer-based injectable sustained-release
       microspheres for peptide and protein drugs)
ΙT
    Functional groups
        (sulfonyl group; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
IT
    Extraction
        (supercrit.; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
    Antigens
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vaccine; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
    9001-99-4
ΙT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (A; prepn. of polymer-based injectable sustained-release
       microspheres for peptide and protein drugs)
    50-21-5, Lactic acid, biological studies
                                                77-92-9,
IΤ
    Citric acid, biological studies
                                       79-14-1, Glycolic acid
     , biological studies
                            87-69-4, Tartaric acid, biological studies
    110-17-8, Fumaric acid, biological studies
                                                  6915-15-7, Malic acid
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (acidifying agent; prepn. of polymer-based injectable
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sustained-release microspheres for peptide and protein drugs)
ΙT
    102-71-6, Triethanolamine, biological studies 111-42-2, Diethanolamine,
    biological studies
                         141-43-5, Monoethanolamine, biological studies
    144-55-8, Sodium bicarbonate, biological studies
                                                       471-34-1, Calcium
    carbonate, biological studies 546-93-0, Magnesium
    carbonate
                994-36-5, Sodium citrate 1309-48-4, Magnesium oxide,
    biological studies
                         6284-40-8, Meglumine
                                               7778-49-6, Potassium citrate
    14987-04-3, Magnesium trisilicate
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (alkalizing agent; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
     9002-64-6, Parathyroid hormone
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (and inhibitors; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
IT
    1066-33-7, Ammonium bicarbonate
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (gas forming agent; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
TT
     9001-12-1, Collagenase
                             9015-94-5, Renin, biological studies
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
ΙT
    105913-11-9, Plasminogen activator
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (kidney; prepn. of polymer-based injectable sustained-release
       microspheres for peptide and protein drugs)
ΙT
     64-19-7, Acetic acid, biological studies
                                               111-86-4, Octylamine
    124-07-2, Caprylic acid, biological studies 1309-42-8,
    Magnesium hydroxide
                         7647-14-5, Sodium chloride,
    biological studies
                         10043-52-4, Calcium chloride, biological studies
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
       microspheres for peptide and protein drugs)
IΤ
    121-54-0, Benzethonium chloride 151-21-3, Sodium lauryl sulfate,
    biological studies 577-11-7, Docusate sodium 1393-25-5, Secretin
                       1402-38-6, Oncostatin 8044-71-1, Cetrimide
    1398-61-4, Chitin
                                             9001-28-9, Factor IX
     9001-25-6, Blood-coagulation factor VII
     9001-63-2, Lysozyme 9002-01-1, Streptokinase
                                                     9002-60-2,
    Adrenocorticotrophic hormone, biological studies
                                                       9002-61-3, Human
                             9002-67-9, Luteinizing hormone
                                                              9002-68-0,
    chorionic gonadotropin
                                   9002-69-1, Relaxin 9002-71-5, Thyroid
     Follicle stimulating hormone
                          9002-72-6, Growth hormone 9002-89-5, Polyvinyl
     stimulating hormone
              9004-10-8, Insulin, biological studies
                                                      9004-53-9, Dextrin
    alcohol
     9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid
     9005-25-8, Starch, biological studies
                                            9005-32-7, Alginic acid
     9005-49-6, Heparin, biological studies
                                            9007-12-9, Calcitonin
                             9007-92-5, Glucagon, biological studies
     9007-27-6, Chondroitin
                                 9012-76-4, Chitosan
    9011-97-6, Cholecystokinin
                                                       9015-71-8,
    Corticotropin releasing factor
                                     9034-39-3, Growth hormone releasing
                                    9039-53-6, Urokinase
             9035-68-1, Proinsulin
                                                            9041 - 92 - 3,
                           9054-89-1, Superoxide dismutase
                                                             9056-36-4,
     .alpha.1-Antitrypsin
                      9061-61-4, Nerve growth factor 11096-26-7,
    Keratan sulfate
                     15802-18-3D, Cyanoacrylic acid, esters, polymers
    Erythropoietin
    24980-41-4, Polycaprolactone 25104-18-1, Poly(L-lysine)
                                                               25248-42-4,
                                   25931-47-9
                                                 26009-03-0, Polyglycolide
    Polycaprolactone
                      25868-59-1
     26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]
                                                           26202-08-4,
                    26680-10-4, Polylactide 26780-50-7, Poly
    Polyglycolide
                            31621-87-1,
     (lactide-co-glycolide)
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Polydioxanone 34346-01-5, Resomer RG 502H
                                                 37221-79-7,
     Vasoactive intestinal polypeptide 38000-06-5, Poly(L-lysine)
                           57285-09-3, Inhibin
     52906-92-0, Motilin
                                                 59392-49-3, Gastric inhibitory
               59763-91-6, Pancreatic polypeptide
                                                    61912-98-9, Insulin-like
     peptide
                     62229-50-9, Epidermal growth factor
                                                           62683-29-8, Colony
     growth factor
     stimulating factor 67763-96-6, Somatomedin C
                                                     77272-10-7, Macrocortin
     80043-53-4, Gastrin releasing peptide
                                             82657-92-9, Prourokinase
     83652-28-2, Calcitonin gene-related peptide
                                                 85637-73-6, Atrial
                          113189-02-9, Antihemophilic factor
                                                               139639-23-9,
     natriuretic factor
     Tissue plasminogen activator
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Bodmer; In J Controlled Release 1992, V211-3, P129
(2) Syntex Inc; US 5470582 1995 HCAPLUS
     546-93-0, Magnesium carbonate
ТТ
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (alkalizing agent; prepn. of polymer-based injectable
        sustained-release microspheres for peptide and protein drugs)
     546-93-0 HCAPLUS
RN
     Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
HO- C- OH
   Mq
     1309-42-8, Magnesium hydroxide
ΤТ
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
RN
     1309-42-8 HCAPLUS
CN
     Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
HO-Mg-OH
     26780-50-7, Poly(lactide-co-
ΙT
     glycolide) 34346-01-5, Resomer RG 502H
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of polymer-based injectable sustained-release
        microspheres for peptide and protein drugs)
RN
     26780-50-7 HCAPLUS
     1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione
CN
     (9CI) (CA INDEX NAME)
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CM 1

CRN 502-97-6 CMF C4 H4 O4

OH $Me-CH-CO_2H$

ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2003 ACS 2001:564791 HCAPLUS L89 ΑN DN 135:121657 Composition for intestinal delivery ΤI IN Vandenberg, Grant William PΑ Aqua Solution Inc., Can. PCT Int. Appl., 62 pp. SO CODEN: PIXXD2 DTPatent LA English ICM A23K001-14 IC

ICS A23K001-16; A23K001-175; A61K047-12; A61K047-18 CC 18-6 (Animal Nutrition) Section cross-reference(s): 17, 63 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE _____ --------------WO 2001-CA73 20010125 WO 2001054514 A1 20010802 PΙ W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG 20021023 EP 2001-902185 EP 1250056 A1 20010125 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR NO 2002003464 A 20020924 NO 2002-3464 20020719 Ρ 20000127 PRAI US 2000-178318P W WO 2001-CA73 20010125 The present invention relates to a new compn., use and method for oral AB administration to a human or an animal of a physiol. active agent comprising neutralizing agents to increase pH in the digestive system to prevent denaturation, inhibitors of digestive enzymes to substantially prevent enzymic digestion, and at least uptake-increasing agents which increases intestinal absorption of a physiol. active agent, a drug and/or a nutrient. ST intestine delivery system nutrient drug; fish feeding expt somatotropin ΙT Plasmids (DNA vectors; compn. for intestinal delivery of nutrients and drugs) TT Antihistamines (H2; compn. for intestinal delivery of nutrients and drugs) IT Immunostimulants (adjuvants; compn. for intestinal delivery of nutrients and drugs) IT Glycosides RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino; compn. for intestinal delivery of nutrients and drugs) TT Fats and Glyceridic oils, biological studies RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (animal; compn. for intestinal delivery of nutrients and drugs) ΙT Nutrients (anti-; compn. for intestinal delivery of nutrients and drugs) TΤ Macrolides RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antibiotics; compn. for intestinal delivery of nutrients and drugs) IΤ Gene, animal RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antigenes; compn. for intestinal delivery of nutrients and drugs) ΙT Rice (Oryza sativa) (bran, physiol. active compds. from; compn. for intestinal delivery of nutrients and drugs) ITActinobacillus Analgesics Antacids Anti-inflammatory agents Antibacterial agents

Antibiotics Antioxidants

Antitumor agents

Bacilli

Bacteria (Eubacteria)

Bacteroides

Bean (Phaseolus vulgaris)

Binders

Bird (Aves)

Brewers' yeast

Campylobacter

Capnocytophaga

Chlamydia

Clostridium

Coliform bacteria

Coloring materials

Corynebacterium

Drug delivery systems

Eikenella

Enterococcus

Erysipelothrix

Eubacterium

Feed additives

Feeding experiment

Fish

Flavor

Flavoring materials

Food additives

Food preservatives

Fungicides

Fusobacteria

Haemophilus

Immunostimulants

Insect (Insecta)

Klebsiella

Lactobacillus

Listeria

Livestock

Lubricants

Mammal (Mammalia)

Micrococcus

Mitsuokella

Moraxella

Mushroom

Mycoplasma

Neisseria

Nutrients

Oncorhynchus mykiss

Parasiticides

Pasteurella

Peptococcus

Peptostreptococcus

Porphyromonas

Poultry

Preservatives

Prevotella

Propionibacterium

Salvelinus fontinalis

Staphylococcus

Streptococcus

Streptomyces

Surfactants

Sweetening agents

Toxicants Tracers Treponema Ureaplasma Vaccines Veillonella Virus Yeast (compn. for intestinal delivery of nutrients and drugs) ΙT Albumins, biological studies Antibodies Bacteriocins Bile salts Blood-coagulation factors Carbohydrates, biological studies Enzymes, biological studies Growth promoters, animal Hormones, animal, biological studies Hydrocarbon oils Immunoglobulins Interferons Interleukins Lecithins Lipids, biological studies Lysophosphatidylcholines Mucopolysaccharides, biological studies Neurotransmitters Neurotrophic factors Ovalbumin Peptides, biological studies Proteins, general, biological studies Saponins Steroids, biological studies Sulfonamides Tetracyclines RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compn. for intestinal delivery of nutrients and drugs) Enzymes, biological studies IΤ RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (digestive, inhibitors of; compn. for intestinal delivery of nutrients and drugs) Acidity ΙT (drugs increasing; compn. for intestinal delivery of nutrients and drugs) ΙT Growth promoters, animal RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (epithelial; compn. for intestinal delivery of nutrients and drugs) Angiogenic factors IT RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (factors inhibiting; compn. for intestinal delivery of nutrients and drugs) ΙT Cell differentiation Cell proliferation (factors; compn. for intestinal delivery of nutrients and drugs) IT Fats and Glyceridic oils, biological studies RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses) (fish; compn. for intestinal delivery of nutrients and drugs) ΙT Nucleic acids RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological

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study); USES (Uses)
        (fragments; compn. for intestinal delivery of nutrients and drugs)
ΙT
     Growth promoters, animal
     RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (nerve growth factor; compn. for intestinal delivery of nutrients and
        drugs)
     Neurohormones
ΙT
     RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (neuromodulators; compn. for intestinal delivery of nutrients and
        drugs)
ΙT
     Seed
        (oilseed, physiol. active compds. from; compn. for intestinal delivery
        of nutrients and drugs)
     Drug delivery systems
TΤ
        (ointments; compn. for intestinal delivery of nutrients and drugs)
IT
     Broad bean (Vicia faba)
     Kidney bean
     Soybean (Glycine max)
     Wheat bran
        (physiol. active compds. from; compn. for intestinal delivery of
        nutrients and drugs)
     Intestinal bacteria
ΙT
        (probiotic; compn. for intestinal delivery of nutrients and drugs)
     Proliferation inhibition
IT
        (proliferation inhibitors; compn. for intestinal delivery of nutrients
        and drugs)
ΙT
        (rice, physiol. active compds. from; compn. for intestinal delivery of
        nutrients and drugs)
ΙT
     Biological transport
        (uptake, agents for improvement of; compn. for intestinal delivery of
        nutrients and drugs)
     Growth promoters, animal
IΤ
     RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (vascular endothelial growth and permeability factor; compn. for
        intestinal delivery of nutrients and drugs)
     Fats and Glyceridic oils, biological studies
ΙT
     RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (vegetable; compn. for intestinal delivery of nutrients and drugs)
     302-95-4, sodium deoxycholate 351199-09-2, Oralject
ΙT
     RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
        (compn. for intestinal delivery of nutrients and drugs)
ΙT
     54-21-7, Sodium salicylate
                                 56-75-7, Chloramphenicol
                                                             60-00-4, EDTA,
                          60-33-3, Linoleic acid, biological studies
     biological studies
     60-54-8D, Tetracycline, derivs.
                                      66-79-5, Oxacillin
                                                            69-53-4, Ampicillin
                                91-22-5D, Quinoline, fluoro derivs.,
     83-44-3, Deoxycholic acid
                          112-80-1, Oleic acid, biological studies
     biological studies
                    144-55-8, Sodium bicarbonate, biological studies
     Erythromycin
                           151-21-3, Sodium lauryl sulfate, biological studies
     147-52-4, Nafcillin
                             154-21-2, Lincomycin
     153-61-7, Cephalothin
                                                   471-34-1, Calcium
                                     497-19-8, Sodium carbonate, biological
     carbonate, biological studies
     studies 546-93-0, Magnesium carbonate
     994-36-5, Sodium citrate 1309-42-8, Magnesium
                1309-48-4, Magnesium oxide, biological studies
     hydroxide
                             1404-26-8, Polymyxin B 1404-90-6, Vancomycin
     1403-66-3, Gentamicin
                             4697-36-3, Carbenicillin
                                                        5892-10-4, Bismuth
     1406-05-9, Penicillin
     subcarbonate
                    7439-95-4D, Magnesium, salts, biological studies
     9002-72-6, Growth hormone
                                 9002-93-1
                                             9005-63-4D, Polyoxyethylene
```

9034-39-3, Somatoliberin

sorbitan, esters

9041-92-3

10043-83-1,

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Magnesium phosphate
                           10103-46-5, Calcium phosphate
                                                          13292-46-1, Rifampin
    14987-04-3, Magnesium trisilicate 15686-71-2, Cephalexin
                                                                  18323-44-9,
                   25496-72-4, Monoolein 26787-78-0, Amoxicillin
    Clindamycin
     32986-56-4, Tobramycin
                              34787-01-4, Ticarcillin
                                                        37091-66-0, Azlocillin
     51481-65-3, Mezlocillin
                             56391-56-1, Netilmicin
                                                        59227-89-3
     61477-96-1, Piperacillin 64221-86-9, Imipenen
                                                       68401-81-0, Ceftizoxime
     69227-93-6, Lauryl-.beta.-D-maltopyranoside
                                                   72558-82-8, Ceftazidime
    73384-59-5, Ceftriaxone 78110-38-0, Aztreonam
                                                       81103-11-9,
                     83869-56-1, GMCSF
                                         83905-01-5, Azithromycin
    Clarithromycin
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (compn. for intestinal delivery of nutrients and drugs)
     9001-75-6, Pepsin
TΤ
                       9014-74-8, Enteropeptidase
     RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inhibitors of; compn. for intestinal delivery of nutrients and drugs)
     9001-92-7, proteinase
TΤ
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inhibitors; compn. for intestinal delivery of nutrients and drugs)
             THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.
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   MEDLINE
(2) Breton, B; JOURNAL OF APPLIED ICHTHYOLOGY 1998, V14(3-4), P251 HCAPLUS
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ΙT
    546-93-0, Magnesium carbonate
    1309-42-8, Magnesium hydroxide
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (compn. for intestinal delivery of nutrients and drugs)
    546-93-0 HCAPLUS
RN
    Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
CN
но-с-он
   Mg
RN
    1309-42-8 HCAPLUS
CN
    Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
HO-Mg-OH
```

2000:36953 HCAPLUS 132:185360 DN TΙ Stabilization of proteins encapsulated in injectable poly(lactide-co-glycolide)

ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2003 ACS

L89

AN

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Zhu, Gaozhong; Mallery, Susan R.; Schwendeman, Steven P.
ΑU
CS
    Colleges of Pharmacy and of Dentistry, The Ohio State University,
     Columbus, OH, 43210, USA
    Nature Biotechnology (2000), 18(1), 52-57 CODEN: NABIF9; ISSN: 1087-0156
SO
PΒ
    Nature America
DT
     Journal
LA
    English
CC
    63-6 (Pharmaceuticals)
    Controlled release from biodegradable polymers is a novel approach to
AB
     replace daily painful injections of protein drugs. A major
     obstacle to development of these polymers is the need to retain the
     structure and biol. activity of encapsulated proteins during months of
     incubation under physiol. conditions. We encapsulated bovine serum
     albumin (BSA) in injectable poly(DL-lactide-
     co-glycolide) (PLGA) 50/50 cylindrical implants and
     detd. the mechanism of BSA instability. Simulations of the polymer
    microclimate revealed that moisture and acidic pH (<3) triggered unfolding
     of encapsulated BSA, resulting in peptide bond hydrolysis and noncovalent
     aggregation. To neutralize the acids liberated by the biodegradable
     lactic/glycolic acid-based polyester, we
     coincorporated into the polymer an antacid, Mg(OH)
    2, which increased microclimate pH and prevented BSA structural
    losses and aggregation for over 1 mo. We successfully applied this
     stabilization approach in both cylinder- and microsphere-
     injectable configurations and for delivery of angiogenic basic
     fibroblast growth factor and bone-regenerating bone morphogenetic
    protein-2.
ST
     stabilization protein polylactide polyglycolide; controlled release
    microsphere polyester stabilization protein
    Bone morphogenetic proteins
TΤ
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (2; stabilization of proteins encapsulated in injectable
       poly(lactide-co-glycolide))
TT
     Polyesters, biological studies
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
    use); BIOL (Biological study); PROC (Process); USES (Uses)
        (dilactone-based; stabilization of proteins encapsulated in
        injectable poly(lactide-co-
        glycolide))
     Drug delivery systems
TT
        (implants; stabilization of proteins encapsulated in injectable
       poly(lactide-co-glycolide))
ΙΤ
     Drug delivery systems
        (microspheres, controlled-release; stabilization of proteins
        encapsulated in injectable poly(lactide-
        co-glycolide))
    Albumins, biological studies
ΙT
    RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
    use); BIOL (Biological study); PROC (Process); USES (Uses)
        (serum; stabilization of proteins encapsulated in injectable
       poly(lactide-co-glycolide))
ΤТ
     Dissolution rate
     Encapsulation
        (stabilization of proteins encapsulated in injectable
        poly(lactide-co-glycolide))
TΤ
     Proteins, general, biological studies
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (stabilization of proteins encapsulated in injectable
        poly(lactide-co-glycolide))
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ΙT 106096-93-9, Basic fibroblast growth factor RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (stabilization of proteins encapsulated in injectable poly(lactide-co-glycolide)) TΤ 1309-42-8, Magnesium hydroxide 26780-50-7, Poly(DL-lactide-coglycolide) RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (stabilization of proteins encapsulated in injectable poly(lactide-co-glycolide)) RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Berscht, P; Biomaterials 1994, V15, P593 HCAPLUS (2) Brunner, A; Pharm Res 1999, V16, P847 HCAPLUS (3) Cleland, J; Pharm Res 1996, V13, P1464 HCAPLUS (4) Cohen, S; Pharm Res 1991, V8, P713 HCAPLUS (5) Costantino, H; J Pharm Sci 1994, V83, P1662 HCAPLUS (6) Crotts, G; J Controlled Release 1997, V47, P101 HCAPLUS (7) Davies, M; Journal of Biomaterial Applications 1997, V12, P31 HCAPLUS (8) Dutta, A; Pharm Med 1993, V7, P9 (9) Edelman, E; Biomaterials 1991, V12, P619 HCAPLUS (10) Edelman, E; Proc Natl Acad Sci 1993, V90, P1513 HCAPLUS (11) Fu, K; Proceedings 25th International Symposium on Controlled Resealse of Bioactive Materials 1998, V25, P150 (12) Fukunaga, K; J Pharm Pharmacol 1994, V46, P168 HCAPLUS (13) Gabra, N; Biochem Biophys Res Commun 1994, V205, P1423 HCAPLUS (14) Gospodarowicz, D; J Cell Physiol 1986, V128, P475 HCAPLUS (15) Heller, J; Biomaterials 1990, V11, P659 HCAPLUS (16) Herrlinger, M; Thesis Univ Heidelberg 1994 (17) Hutchinson, F; J Controlled Release 1990, V13, P279 HCAPLUS (18) Johnson, O; Nat Med 1996, V2, P795 HCAPLUS (19) Kenley, R; Pharm Res 1993, V10, P1393 HCAPLUS (20) Langer, R; Nature 1976, V263, P797 HCAPLUS (21) Li, S; J Mater Sci 1990, V1, P123 HCAPLUS (22) Liu, W; Biotechnol Bioeng 1991, V37, P177 HCAPLUS (23) Mader, K; Biomaterials 1996, V17, P457 HCAPLUS (24) Mader, K; Pharm Res 1998, V15, P787 HCAPLUS (25) Manning, M; Pharm Res 1989, V6, P903 HCAPLUS (26) Mayer, M; Plast Reconstr Surg 1996, V98, P247 MEDLINE (27) Ogawa, Y; J Pharm Pharmcol 1989, V41, P439 HCAPLUS (28) Okada, H; Pharm Res 1994, V11, P1143 HCAPLUS (29) Peters, T; Adv Protein Chem 1985, V37, P161 HCAPLUS (30) Putney, S; Nat Biotechnol 1998, V16, P153 HCAPLUS (31) Schwendeman, S; Controlled drug delivery 1997, P229 HCAPLUS (32) Schwendeman, S; J Microencapsulation 1998, V15, P299 HCAPLUS (33) Schwendeman, S; Microparticulate systems for the delivery of proteins and vaccines 1996, P1 HCAPLUS (34) Schwendeman, S; Proc Natl Acad Sci 1995, V92, P11234 HCAPLUS (35) Shenderova, A; Pharm Res 1997, V14, P1406 HCAPLUS (36) Shenderova, A; Pharm Res 1999, V16, P241 HCAPLUS (37) Sommer, A; J Cell Physiol 1989, V138, P215 HCAPLUS (38) Struck, M; Bio/Technology 1994, V12, P674 MEDLINE (39) Sullivan, R; J Tiss Culture Methods 1986, V10, P125 HCAPLUS (40) Talmadge, J; Adv Drug Delivery Rev 1993, V10, P247 HCAPLUS (41) Wang, E; Proc Natl Acad Sci 1990, V87, P2220 HCAPLUS (42) Wang, Y; Formulation, characterization, and stability of protein drugs 1996, P141 (43) Watanabe, H; Biochem Biophys Res Commun 1991, V175, P229 HCAPLUS

(44) Welch, R; J Bone Miner Res 1998, V13, P1483 HCAPLUS (45) Zhang, X; J Controlled Release 1993, V25, P61 HCAPLUS

```
ΙT
     1309-42-8, Magnesium hydroxide
     26780-50-7, Poly(DL-lactide-co-
     glycolide)
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (stabilization of proteins encapsulated in injectable
        poly(lactide-co-glycolide))
     1309-42-8 HCAPLUS
RN
     Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
CN
HO-Mg-OH
RN
     26780-50-7 HCAPLUS
CN
     1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione
     (9CI) (CA INDEX NAME)
     CM
          1
     CRN
          502-97-6
     CMF C4 H4 O4
         , 0
    , O.
     0
     CM
          2
         95-96-5
     CRN
         C6 H8 O4
     CMF
      0
   Ö
           Ме
      0
    ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
AN
     1998:527193 HCAPLUS
DN
     129:166193
TТ
     Therapeutic treatment and prevention of infections with a bioactive
     material encapsulated within a biodegradable-biocompatible polymeric
     matrix
     Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot;
ΙN
     Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas
     R.; Roberts, F. Donald; Friden, Phil
     United States Dept. of the Army, USA; Van Hamont, John E.; et al.
PA
SO
     PCT Int. Appl., 363 pp.
     CODEN: PIXXD2
     Patent
DT
LA
     English
IC
     ICM A61K009-52
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ICS A61K047-30
    63-5 (Pharmaceuticals)
CC
    Section cross-reference(s): 1, 2, 15
FAN.CNT 12
    PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
                    ----
                                         ______
     ______
                    A1 19980730 WO 1998-US1556 19980127
    WO 9832427
PΙ
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
            UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
            GA, GN, ML, MR, NE, SN, TD, TG
                    B1 20011030
                                         US 1997-789734 19970127
    US 6309669
    AU 9863175
                     A1 19980818
                                         AU 1998-63175 19980127
PRAI US 1997-789734
                   Α
                          19970127
    US 1984-590308 B1 19840316
    US 1992-867301 A2 19920410
    US 1995-446148
                   A2 19950522
    US 1995-446149 B2 19950522
                   B2 19960124
    US 1996-590973
    WO 1998-US1556 W
                          19980127
    Novel burst-free, sustained release biocompatible and biodegradable
AΒ
    microcapsules are disclosed which can be programmed to release their
    active core for variable durations ranging from 1-100 days in an aq.
    physiol. environment. The microcapsules are comprised of a core of
    polypeptide or other biol. active agent encapsulated in a matrix of poly(
    lactide/glycolide) copolymer, which may
    contain a pharmaceutically acceptable adjuvant, as a blend of
    upcapped free carboxyl end group and end-capped forms ranging in ratios
    from 100/0 to 1/99.
    infection microcapsule sustained release peptide copolymer
ST
        (B, chronic; prevention of infections with a bioactive material
       encapsulated within a biodegradable-biocompatible polymeric matrix)
ΙT
    Hepatitis
        (C, chronic; prevention of infections with a bioactive material
       encapsulated within a biodegradable-biocompatible polymeric matrix)
ΙT
    Trypanosoma cruzi
        (Chagas' disease from; prevention of infections with a bioactive
       material encapsulated within a biodegradable-biocompatible polymeric
       matrix)
ΙT
    Immunoglobulins
    RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
    study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
     (Process)
        (G, ampicillin-specific; prevention of infections with a bioactive
       material encapsulated within a biodegradable-biocompatible polymeric
       matrix)
IT
    Nervous system
        (Huntington's chorea; prevention of infections with a bioactive
       material encapsulated within a biodegradable-biocompatible polymeric
       matrix)
ΙT
    Antitumor agents
    Antitumor agents
        (Kaposi's sarcoma; prevention of infections with a bioactive material
       encapsulated within a biodegradable-biocompatible polymeric matrix)
ΙT
        (acrosome, proteinase of; prevention of infections with a bioactive
```

material encapsulated within a biodegradable-biocompatible polymeric

matrix)

ΙT Diagnosis (agents; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Ragweed (Ambrosia) (allergy; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT (amebiasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Antibiotics (aminoglycoside; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TT Absidia ramosa Actinobacillus equuli Actinobacillus seminis Arcanobacterium pyogenes Aspergillus fumigatus Babesia caballi Brucella melitensis Campylobacter fetus Campylobacter fetus intestinalis Candida albicans Candida tropicalis Chlamydia psittaci Clostridium tetani Equid herpesvirus 1 Equine arteritis virus Escherichia coli Gardnerella vaginalis Human herpesvirus 1 Human herpesvirus 2 Leptospira interrogans pomona Listeria monocytogenes Mycobacterium tuberculosis Mycoplasma bovigenitalium Mycoplasma hominis Neisseria gonorrhoeae Pneumocystis carinii Pseudomonas aeruginosa Rhodococcus equi Salmonella abortivoequina Salmonella abortusovis Streptococcus group B Toxoplasma gondii Treponema pallidum Trichomonas vaginalis Tritrichomonas foetus Trypanosoma equiperdum (antigens of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Mycobacterium (antimycobacterial agents; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TT Mouth Mouth (aphthous ulcer; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Drugs Drugs (appetite stimulants; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric

matrix)

Heart, disease TΤ (arrhythmia; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Blood vessel IT(artificial, infections surrounding; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Dermatitis (atopic; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Babesia (babesiasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TT Skin, neoplasm Skin, neoplasm (basal cell carcinoma, inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Antitumor agents Antitumor agents Skin, neoplasm (basal cell carcinoma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Natural products, pharmaceutical RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (belladonna; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Prostate gland (benign hyperplasia; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Polymers, biological studies IΤ RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (biodegradable; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Nervous system (central, disease; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Polymers, biological studies TΤ RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (co-; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Intestine, disease (colitis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Antigens RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (colony factor; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Intestine, neoplasm Intestine, neoplasm (colorectal, inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric

matrix)

TΨ Antitumor agents Antitumor agents Intestine, neoplasm (colorectal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Thrombosis (coronary arterial; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Artery, disease (coronary, thrombosis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Vasodilators ΤТ (coronary; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Tapeworm (Cestoda) (cysticercosis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT (cystitis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Mental disorder (depression; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT (diabetic retinopathy; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Polyesters, biological studies IT RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (dilactone-based; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Digestive tract (drugs for; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT(edema, peritumoral; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Drug delivery systems (emulsions; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT B cell (lymphocyte) T cell (lymphocyte) (epitopes of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΨ Alkaloids, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (ergot; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Amino acids, biological studies IΤ Fats and Glyceridic oils, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (essential; prevention of infections with a bioactive material

encapsulated within a biodegradable-biocompatible polymeric matrix)

Fasciola TΤ (fascioliasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Filaria (filariasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Anthelmintics TT (filaricides; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Digestive tract (gastroenteritis, virus causing; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TT Intestine, disease (giardiasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Transplant and Transplantation (graft-vs.-host reaction; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Calymmatobacterium granulomatis ΙT (granuloma inguinale from, antigens of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Antigens TT RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (hepatitis B surface; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Liver, neoplasm (hepatoma, inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Antitumor agents ΤТ Liver, neoplasm (hepatoma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΤТ Human herpesvirus 2 (herpes genitalis from; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Human herpesvirus 3 (herpes zoster from, antigens of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Parvovirus Retroviridae (human; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Globulins, biological studies RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (hyperimmune; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Sexual behavior IT (impotence; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Eye, disease Eye, disease Mouth

Mouth

Skin, disease

(infection; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Prosthetic materials and Prosthetics IT (infections surrounding; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Drug delivery systems (inhalants; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Fertility Ovary, neoplasm Pancreas, neoplasm Pancreas, neoplasm (inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Drug delivery systems (injections; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric ΙT Diabetes mellitus (insulin-dependent; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT(leishmaniasis from, visceral; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Antitumor agents (lung small-cell carcinoma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Antibiotics IT (macrolide; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Antitumor agents (mammary gland; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Antitumor agents (melanoma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΤТ Drug delivery systems (microcapsules; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Drug delivery systems (microspheres; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Drug delivery systems ΙT (nasal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΤT Mammary gland Prostate gland (neoplasm, inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Mammary gland ΙT Prostate gland (neoplasm; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Meningitis (neoplastic; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

ΙT

Angiogenesis Angiogenesis Angiogenesis (neovascularization, retinal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Diabetes mellitus

(non-insulin-dependent; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Anti-inflammatory agents

(nonsteroidal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Emulsions

(oil-in-water; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(oral; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Nitrites

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(org.; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Antitumor agents

(ovary; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Antitumor agents

Antitumor agents

(pancreas; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Anxiety

IT

ΙT

(panic disorder; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Paragonimus

(paragonimiasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Hormones, animal, biological studies
PI: RPP (Biological process): BSU (Bi

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(peptide; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Periodontium

(periodontitis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Mental disorder

(phobia; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Adhesion, biological

(postsurgical; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT AIDS (disease)

Acinetobacter
Actinomycetales
Adenoviridae
Adrenoceptor agonists
Aerococcus
Aeromonas
Allergy inhibitors
Alzheimer's disease
Analgesics
Anesthetics

Angiogenesis

Angiogenesis inhibitors

Anthelmintics

Anti-infective agents

Anti-inflammatory agents

Antiarrhythmics

Antiarthritics

Antibacterial agents

Antibiotics

Anticholesteremic agents

Anticoagulants

Anticoagulants

Anticonvulsants

Antidepressants

Antidiabetic agents

Antidiarrheals

Antiemetics

Antihistamines

Antihypertensives

Antimalarials

Antimigraine agents

Antiparkinsonian agents

Antipyretics

Antirheumatic agents

Antiserums

Antitumor agents

Antitussives

Antiulcer agents

Antiviral agents

Appetite depressants

Arbovirus

Arcanobacterium haemolyticum

Arenavirus

Asthma

Bacillus (bacterium genus)

Biocompatibility

Blood substitutes

Bordetella

Borrelia

Bronchodilators

Brucella

Cachexia

Calymmatobacterium

Campylobacter

Cardiopulmonary bypass

Cardiotonics

Cardiovascular agents

Cholinergic agonists

Clostridium

Contraceptives

Coronavirus

Corynebacterium

Cryptosporidium parvum

Cystic fibrosis

Cytomegalovirus

Cytotoxic agents

Decongestants

Diagnosis

Diarrhea

Dissolution rate

Diuretics

Drug bioavailability

Drug dependence

Ebola virus

Echinococcus

Electrolytes, biological

Emulsifying agents

Enterobacteriaceae

Enterococcus

Enterovirus

Epitopes

Erysipelothrix

Expectorants

Filovirus

Flavobacterium

Freeze drying

Fungicides

Gardnerella

Gram-negative bacteria

Gram-positive bacteria (Firmicutes)

Haemophilus

Haemophilus ducreyi

Helicobacter

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Human herpesvirus 3

Human herpesvirus 4

Human immunodeficiency virus

Human immunodeficiency virus 1

Human parainfluenza virus

Human poliovirus

Hypercholesterolemia

Hypnotics and Sedatives

Immunization

Immunomodulators

Immunostimulants

Infection

Influenza virus

Kidney, disease

Lactococcus

Legionella

Leptospira

Leuconostoc

Listeria

Measles virus

Melanoma

Micrococcus

Molluscum contagiosum virus

Moraxella

Multiple sclerosis

Mumps virus

Muscle relaxants

Narcotics

Neisseria

Nervous system agents

Nutrients

Opioid antagonists

Osteoarthritis

Osteomyelitis

Osteoporosis

Ovary, neoplasm

Pancreas, neoplasm

Papillomavirus

Parasiticides

Parkinson's disease

Pediococcus Planococcus (bacterium) Plesiomonas Pneumonia Poxviridae Pseudomonas Psoriasis Psychotropics Rabies virus Reoviridae Respiratory syncytial virus Rheumatoid arthritis Rhinovirus Rhodococcus Rotavirus Rothia (bacterium) Rubella virus Salmonella typhi Sexually transmitted diseases Shigella boydii Shigella dysenteriae Shigella flexneri Shigella sonnei Spirillum Staphylococcus Streptobacillus Streptococcus Thrombosis Tranquilizers Treponema Vaccines Vasodilators Vibrio Vibrio cholerae Wolinella succinogenes Yersinia (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Alkaloids, biological studies Antibodies Antigens Enzymes, biological studies Estrogens Glycolipids Glycopeptides Growth factors, animal Lipopolysaccharides Peptides, biological studies Pheromones, animal Progestogens Prostaglandins Proteins, general, biological studies Steroids, biological studies Sulfonamides Tetracyclines Vitamins RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) Drug delivery systems

ΙT

ΙT

(prodrugs; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Proliferation inhibition

(proliferation inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Antitumor agents

(prostate gland; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Pilus

(proteins; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Scalp

(psoriasis of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(rectal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Artery, disease

(restenosis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Eye, disease

Eye, disease

Eye, disease

(retina, neovascularization; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Schistosoma

(schistosomiasis from; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Lung, neoplasm

(small-cell carcinoma, inhibitors; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Lung, neoplasm

(small-cell carcinoma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Muscle relaxants

(spasmolytics; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Contraceptives

(spermicidal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Brain, disease

(spongiform encephalopathy, agent causing; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Appetite

Appetite

(stimulants; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Brain, disease

(stroke; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Strongylus

(strongylodiasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(sustained-release, programmable; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

ΙT Osteoporosis (therapeutic agents; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT (therapy with; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Drug delivery systems (topical; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Muscle, disease (torticollis, spasmodic; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Toxocara (toxocariasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Toxoplasma qondii (toxoplasmosis from; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Drug delivery systems (transdermal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT (trauma; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Trichinella (trichinellosis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) IT Trichomonas (trichomoniasis; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Drug delivery systems (vaginal; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) ΙT Emulsions (water-in-oil; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) TΤ Lactams RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.beta.-, antibiotics; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 9002-72-6, Somatotropin ΙT RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (deficiency; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 9005-49-6, Heparin, biological studies ΙT RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (neutralization of; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 37326-33-3, Hyaluronidase IT 9001-60-9, Lactate dehydrogenase RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (of sperm; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin ΙT 50-23-7, Hydrocortisone 50-24-8, 50-18-0, Cyclophosphamide 50-33-9, 50-28-2, 17.beta.-Estradiol, biological studies Prednisolone Phenylbutazone, biological studies 50-52-2, Thioridazine 50-55-5, 50-78-2, Aspirin 51-55-8, Atropine, biological studies Reserpine

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52-24-4, Thiotepa
                   52-76-6, Lynestrenol
                                          53-03-2, Prednisone
                                                                53-16-7,
Estrone, biological studies 53-86-1, Indomethacin 54-11-5, Nicotine
55-48-1, Atropine sulfate 55-63-0, Nitroglycerin
                                                    55-86-7, Nitrogen
mustard
          56-53-1, Diethyl stilbestrol 56-75-7, Chloramphenicol
57-27-2, Morphine, biological studies
                                       57-33-0, Sodium pentobarbital
57-42-1, Meperidine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-85-2, Testosterone propionate 57-92-1, Streptomycin a, biological
         58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine
studies
58-22-0
          58-25-3, Chlordiazepoxide 58-39-9, Perphenazine
                                                             58-73-1,
Diphenhydramine
                 59-01-8, Kanamycin a 59-05-2, Methotrexate
                                                                59-92-7,
L-Dopa, biological studies 61-33-6, Penicillin g, biological studies
67-20-9, Nitrofurantoin 68-22-4, Norethisterone 68-23-5, Norethynodrel
69-09-0, Chlorpromazine hydrochloride
                                       69-53-4, Ampicillin
                                                             69-72-7D,
Salicylic acid, derivs. 71-58-9, Medroxyprogesterone acetate
                                                                72-33-3,
Mestranol
           76-57-3, Codeine
                              79-57-2, Oxytetracycline
                                                         79-64-1,
               91-81-6, Tripelennamine 103-90-2, Acetaminophen
Dimethisterone
113-15-5, Ergotamine 114-07-8, Erythromycin
                                             114-49-8, Hyoscine
             121-54-0 122-09-8, Phentermine 125-29-1,
hydrobromide
                 125-71-3, Dextromethorphan 127-48-0, Trimethadione
Dihydrocodeinone
128-62-1, Noscapine 145-94-8, Chlorindanol 148-82-3, Melphalan
155-41-9, Methscopolamine bromide 288-32-4D, Imidazole, derivs.
297-76-7, Ethynodiol diacetate 302-22-7, Chlormadinone acetate
                        309-43-3, Sodium secobarbital 315-30-0,
305-03-3, Chlorambucil
             434-03-7, Ethisterone 439-14-5, Diazepam 443-48-1,
Allopurinol
               469-62-5 471-34-1, Calcium carbonate, biological studies
Metronidazole
497-19-8, Sodium carbonate, biological studies 523-87-5, Dimenhydrinate
546-93-0, Magnesium carbonate 578-66-5D,
8-Aminoquinoline, derivs. 578-68-7D, 4-Aminoquinoline, derivs.
595-33-5, Megestrol acetate 738-70-5, Trimethoprim 846-50-4, Temazepam
1397-89-3, Amphotericin b 1397-94-0, Antimycin a 1403-66-3, Gentamicin
1404-26-8, Polymyxin b 1404-90-6, Vancomycin 4696-76-8, Kanamycin b
5588-33-0, Mesoridazine 5633-18-1, Melengestrol 5786-21-0, Clozapine
5800-19-1, Metiapine 6533-00-2, Norgestrel 7447-40-7, Potassium
chloride (KCl), biological studies 8063-07-8, Kanamycin 9000-83-3,
        9000-92-4, Amylase
                            9001-62-1, Lipase
                                                 9001-63-2, Muramidase
Atpase
9001-67-6, Neuraminidase 9001-78-9, Alkaline phosphatase 9001-99-4,
                                                      9002-07-7, Trypsin
Ribonuclease
              9002-02-2, Succinic acid dehydrogenase
9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies
9025-82-5, Phosphodiesterase
                              9029-12-3, Glutamic acid dehydrogenase
9035-74-9, Glycogen phosphorylase 9046-27-9, .gamma.-
Glutamyltranspeptidase
                        9079-67-8
                                   10118-90-8, Minocycline 11111-12-9,
Cephalosporins 13292-46-1, Rifampin 14271-04-6 21645-51-2, Aluminum
hydroxide, biological studies 22232-71-9, Mazindol
                                                      24730-10-7,
Dihydroergocristine methanesulfonate 25447-66-9 26780-50-7,
Poly(lactide co-glycolide)
26787-78-0, Amoxicillin 30516-87-1, Azt 32986-56-4, Tobramycin
35189-28-7, Norgestimate 37205-61-1, Proteinase inhibitor 37517-28-5,
         53678-77-6D, Muramyl dipeptide, derivs. 53994-73-3, Cefaclor
Amikacin
55268-75-2, Cefuroxime
                       61036-62-2, Teicoplanin 64221-86-9, Imipenem
80738-43-8, Lincosamide 81103-11-9, Clarithromycin 82419-36-1,
          85721-33-1, Ciprofloxacin
Ofloxacin
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV
(Device component use); PEP (Physical, engineering or chemical process);
THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES
(Uses)
   (prevention of infections with a bioactive material encapsulated within
   a biodegradable-biocompatible polymeric matrix)
115966-68-2, Histatin 5 (human parotid saliva)
                                               127716-52-3, Histatin 9
                        174270-18-9, 5-25-Histatin 6 (human parotid
(human parotid saliva)
                                                  211118-03-5
         186138-55-6
                       186138-60-3
                                     194017-97-5
saliva)
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP
(Physical, engineering or chemical process); PRP (Properties); THU
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(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

ΙT

(prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 9007-12-9, Calcitonin 9002-60-2, Adrenocorticotropin, biological studies TT 62229-50-9, Epidermal growth factor 9034-40-6, Lhrh 123781-17-9, Histatin RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 9005-65-6, Tween 80 ΙT 9005-64-5, Tween 20 9005-67-8, Tween 60 106392-12-5, Pluronic RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 75-09-2, uses TΤ RL: NUU (Other use, unclassified); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 146553-70-0 146553-71-1 146553-72-2 146553-73-3 146553-69-7 ΤТ 146553-77-7 146553-78-8 146553-74-4 146553-75-5 146553-76-6 146553-81-3 146553-82-4 146553-83-5 146553-85-7 146553-86-8 146553-90-4 146553-91-5 146553-87-9 146553-88-0 146553-89-1 146553-92-6 164583-46-4 164583-50-0 164583-51-1 211118-14-8 211118-17-1 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix) 1406-05-9D, Penicillin, derivs. ΙT RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix) THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT RF. (1) Jeyanthi; Proceedings International Symposium on Controlled Release of Bioactive Materials 1996, P351 HCAPLUS (2) Oppenheim; US 5486503 A 1996 HCAPLUS (3) Syntex U S AInc; EP 0052510 B2 1994 HCAPLUS (4) Wang; J of Controlled Release 1991, V17, P23 HCAPLUS (5) Yan; J of Controlled Release 1994, V32(3), P231 HCAPLUS (6) Yeh; A Novel Emulsification-Solvent Extraction Technique for Production of Protein Loaded Biodegradable Microparticles for Vaccine and Drug Delivery 1995, V33(3), P437 HCAPLUS ΙT 546-93-0, Magnesium carbonate 26780-50-7, Poly(lactide coglycolide) RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)

RN

CN

546-93-0 HCAPLUS

О || НО— С— ОН

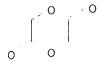
Mg

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

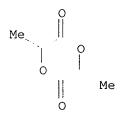
CM 1

CRN 502-97-6 CMF C4 H4 O4



CM 2

CRN 95-96-5 CMF C6 H8 O4



L89 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:481792 HCAPLUS

DN 129:221097

TI Stabilization of bovine serum albumin encapsulated in **injectable poly**(**lactide-co-glycolide**) millicylinders

AU Zhu, G.; Schwendeman, S. P.

- CS Division of Pharmaceutics, The Ohio State University, Columbus, OH, 43210, USA
- SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 267-268 CODEN: PCRMEY; ISSN: 1022-0178
- PB Controlled Release Society, Inc.

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

AB The incomplete protein release from PLGA millicylinders was caused by the formation of water-insol. noncovalent bonded BSA aggregates. The addn. of a base, Mg(OH)2, stabilized the protein by

```
neutralizing the acidic microclimate which was the major source of
     formation of the aggregates.
    polylactide polyglycolide millicylinder serum albumin stabilization
ST
     Polyesters, biological studies
ΙT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (hydroxycarboxylic acid-based; stabilization of serum albumin
        encapsulated in injectable poly(lactide-
        co-glycolide) millicylinders)
    Albumins, biological studies
IT
    RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
    use); BIOL (Biological study); PROC (Process); USES (Uses)
        (serum; stabilization of serum albumin encapsulated in
        injectable poly(lactide-co-
        glycolide) millicylinders)
     Dissolution rate
TT
        (stabilization of serum albumin encapsulated in injectable
        poly(lactide-co-glycolide)
        millicylinders)
     1309-42-8, Magnesium hydroxide
TT
     34346-01-5, Glycolic acid-lactic
    acid copolymer
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (stabilization of serum albumin encapsulated in injectable
        poly(lactide-co-glycolide)
        millicylinders)
    1309-42-8, Magnesium hydroxide
TΤ
     34346-01-5, Glycolic acid-lactic
    acid copolymer
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (stabilization of serum albumin encapsulated in injectable
        poly(lactide-co-glycolide)
        millicylinders)
     1309-42-8 HCAPLUS
RN
    Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
CN
HO-Mg-OH
    34346-01-5 HCAPLUS
RN
     Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA
CN
    INDEX NAME)
    CM
          1
    CRN 79-14-1
    CMF C2 H4 O3
HO-C-CH2-OH
          2
     CM
     CRN 50-21-5
     CMF C3 H6 O3
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ОН

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Me-CH-CO2H
    ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
ΑN
    1998:293361 HCAPLUS
DN
    128:326543
ΤI
    Oral vaccines for young animals with an enteric coating
ΙN
    Gerber, Jay Dean
    Pfizer Inc., USA; Gerber, Jay Dean
PA
SO
    PCT Int. Appl., 22 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
    ICM A61K009-28
IC
    ICS A61K039-15; A61K039-175; A61K039-215; A61K039-23
CC
    63-6 (Pharmaceuticals)
FAN.CNT 1
    PATENT NO.
                     KIND DATE
                                          APPLICATION NO.
                                                           DATE
                           _____
                                                          _____
     ______
                     ____
                                          _____
    WO 9818453
                    A1
                           19980507
ΡI
                                        WO 1997-IB1136 19970922
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
            YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
            GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
            GN, ML, MR, NE, SN, TD, TG
                                          AU 1997-41333
    AU 9741333
                     A1 19980522
                                                           19970922
                                          ZA 1997-9592
    ZA 9709592
                          19990428
                                                           19971027
                      Α
PRAI US 1996-28802P
                           19961028
                      Ρ
    WO 1997-IB1136
                     W
                           19970922
AR
    The present invention provides a vaccine formulation and method ·
    for oral vaccination of animals of weaning age or younger
    against a pathogen in the presence of interfering maternal antibodies.
    The formulation of the invention comprises an antigen in an enteric
    coating. An oral vaccine was prepd. from lactose, Ac-Di-Sol, Mg
    stearate, and lyophilized canine parvovirus that had been attenuated.
ST
    oral vaccine enteric coating
TΤ
    Canine coronavirus
    Canine distemper virus
    Canine parvovirus
    Canine rotavirus
    Gums and Mucilages
        (oral vaccines for young animals with an enteric coating)
IT
    Antigens
    Gelatins, biological studies
    RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
    use); BIOL (Biological study); PROC (Process); USES (Uses)
        (oral vaccines for young animals with an enteric coating)
ΙT
    Vaccines
        (oral; oral vaccines for young animals
       with an enteric coating)
IT
    Drug delivery systems
        (tablets, enteric-coated; oral vaccines for young animals
       with an enteric coating)
                                                             69-65-8,
IT
    57-50-1, Sucrose, biological studies 63-42-3, Lactose
    Mannitol
               69-79-4, Maltose 471-34-1, Calcium carbonate, biological
    studies 546-93-0, Magnesium carbonate
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foley - 09 / 925635 557-04-0, Magnesium stearate 1309-48-4, Magnesium oxide, biological 7778-18-9, Calcium sulfate 9004-34-6D, Cellulose, derivs., biological studies 9005-25-8, Starch, biological studies 14807-96-6, Talcum, biological studies 25086-15-1, Eudragit S100 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (oral vaccines for young animals with an enteric coating) RE.CNT THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) American Home Prod; EP 0181117 A 1986 HCAPLUS (2) Goodnow, R; US 4152413 A 1979 (3) Ulasov, V; RU 2045960 C 1995 HCAPLUS (4) Warner Lambert Co; EP 0420459 A 1991 HCAPLUS 546-93-0, Magnesium carbonate TT RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (oral vaccines for young animals with an enteric coating) 546-93-0 HCAPLUS RN Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME) CN 0 HO-C-OH Mg ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2003 ACS L89 1996:43039 HCAPLUS ΑN

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124:84901
DN
ΤI
     Compositions of transactivating proteins of human immunodeficiency virus
IN
     Goldstein, Gideon; Culler, Michael D.; Shenbagamurthi, Ponniah
     Immunobiology Research Institute, Inc., USA
PA
     PCT Int. Appl., 53 pp.
SO
     CODEN: PIXXD2
     Patent
DT
LA
     English
IC
     ICM A61K039-116
     ICS C07K005-00; C07K007-00; C07H019-00; C07H019-22
CC
     15-2 (Immunochemistry)
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                                 APPLICATION NO.
                                                                      DATE
                                                  -----
PΙ
     WO 9531999
                          A1
                                19951130
                                                 WO 1995-US6077
                                                                      19950516
              AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE,
          KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UZ, VN

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
               SN, TD, TG
                                                 CA 1995-2190972
     CA 2190972
                                19951130
                                                                      19950516
                          AΑ
     AU 9526382
                          A1
                                19951218
                                                  AU 1995-26382
                                                                      19950516
                                                  EP 1995-921262
     EP 767678
                          Α1
                                19970416
                                                                      19950516
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
PRAI US 1994-247991
                                19940523
     WO 1995-US6077
                                19950516
     The inventions provides compns. and a novel method of immunization
AΒ
     directed against released transactivating (TAT) proteins of certain target
     viruses that are taken up by other cells, including particularly HIV and
```

other integrating and chronically infecting viruses. The method employs TAT immunogens, which are capable of eliciting high titer antibody to the native TAT protein, esp. the regions involved in cellular uptake. In example, SIV and HIV-1 TAT peptides and multiple antigenic peptides were synthesized. The multiple antigenic peptides were combined with alum adjuvant for immunization in monkeys, and the antibody titers produced in these monkeys were evaluated.

ST TAT protein multiple antigenic peptide; HIV1 SIV vaccine TAT multiple antigen

IT Liposome

(adjuvant; prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as vaccine for HIV-1 and SIV)

IT Alums

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adjuvant; prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as vaccine for HIV-1 and SIV)

IT Antigens

RL: PRP (Properties)

(multiple antigenic peptide SIV-TAT80-95; prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT Protein sequences

Vaccines

(prepn. of **synthetic** peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT Gene, animal

RL: PRP (Properties)

(TAT, prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT Immunostimulants

(adjuvants, prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as vaccine for HIV-1 and SIV)

IT Ribonucleic acid formation factors

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene tat, prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT Virus, animal

(human immunodeficiency 1, prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT Virus, animal

(simian immunodeficiency, prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

IT 1309-42-8, Magnesium hydroxide

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adjuvant; prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as vaccine for HIV-1 and SIV)

IT 172593-38-3 172593-39-4

RL: PRP (Properties)

(amino acid sequence; prepn. of synthetic peptides and multiple antigenic peptide of TAT protein as **vaccine** for HIV-1 and SIV)

172548-00-4P 172548-01-5P 172548-02-6P 172548-03-7P 172548-04-8P ΙT 172548-07-1P 172548-08-2P 172548-09-3P 172548-05-9P 172548-06-0P 172548-10-6P 172548-11-7P 172548-12-8P 172548-13-9P 172548-14-0P

```
172548-16-2P
                                  172548-17-3P
                                                172548-18-4P 172548-19-5P
    172548-15-1P
    172548-20-8P 172548-21-9P 172548-22-0P 172548-23-1P
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
    study); PREP (Preparation); USES (Uses)
        (prepn. of synthetic peptides and multiple antigenic peptide of TAT
       protein as vaccine for HIV-1 and SIV)
    1309-42-8, Magnesium hydroxide
TΤ
    RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (adjuvant; prepn. of synthetic peptides and multiple
       antigenic peptide of TAT protein as vaccine for HIV-1 and
       SIV)
RN
    1309-42-8 HCAPLUS
CN
    Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
HO-Mq-OH
L89 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2003 ACS
AN
    1992:636699 HCAPLUS
DN
    117:236699
    Preparation of chemically pure and sterile carbon dioxide for subcutaneous
TΙ
    injection
ΙN
    Biro, Istvan; Czipczer, Otto; Demeter, Andras; Piller, Istvan
PA
SO
    Hung. Teljes, 17 pp.
    CODEN: HUXXBU
DT
    Patent
LA
    Hungarian
IC
    ICM C01B031-20
    ICS A61M037-00
CC
     49-8 (Industrial Inorganic Chemicals)
    Section cross-reference(s): 63
FAN.CNT 1
                   KIND DATE
                                         APPLICATION NO. DATE
    PATENT NO.
     ______
                                         _____
    HU 58649 A2 19920330
                                         HU 1990-163
PΙ
                                                         19900116
PRAI HU 1990-163
                          19900116
    Chem. pure and sterile CO2 for s.c. injection is prepd. by
    reacting satd. carbonate or hydrocarbonate solns. With a nontoxic acid in
    sterilized vessels. The evolving CO2 is stored in reaction vessels or
    collected in a syringe for immediate injection. A convenient
    alternative consists in mixing anhyd. or crystd. acids and carbonates in a
    sterilized elastic plastic container sealed with a rubber stopper. CO2
    gas is generated by introducing distd. water through the rubber stopper by
    an injection needle connected to a syringe in which the gas is
     collected for subsequent injection. The nontoxic acids are
     selected from citric, acetic, succinic, tartaric, salicylic, lactic
    phosphonic, or benzoic acids while the carbonates are chosen from Na2CO3,
    NaHCO3, K2CO3, KHCO3, Ca(HCO3)2, or Mg(HCO3)2. The vessels and materials
    are sterilized in autoclave at 120.degree. for 20 min combined with air
    removal by a vacuum pump. The method is esp. suitable for on-site, lab.
    and clin. use, and eliminates the storage and handling of pressurized CO2.
ST
    carbon dioxide sterile pure manuf; injection sterile pure carbon
    dioxide; acid reaction carbonate carbon dioxide
ΙΤ
    Pharmaceutical dosage forms
        (injections, s.c., carbon dioxide for,
       manuf. of pure sterile, by reaction of carbonates with nontoxic acids)
ΙT
     124-38-9P, Carbon dioxide, preparation
    RL: PREP (Preparation)
        (prepn. of pure sterile, by reaction of carbonates with nontoxic acids,
```

for s.c. injection) 50-21-5, Lactic acid, reactions 64-19-7, Acetic ITacid, reactions 65-85-0, Benzoic acid, reactions 69-72-7, reactions 77-92-9, Citric acid, reactions 87-69-4, Tartaric acid, reactions 110-15-6, Succinic acid, reactions 7664-38-2, Phosphoric acid, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with carbonates, pure sterile carbon dioxide prepn. by, for s.c. injection) 144-55-8, Sodium bicarbonate, reactions 298-14-6, Potassium bicarbonate IT497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 2090-64-4 3983-19-5 RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with nontoxic acids, pure sterile carbon dioxide prepn. by, for s.c. injection) ΙT 2090-64-4 RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with nontoxic acids, pure sterile carbon dioxide prepn. by, for s.c. injection) 2090-64-4 HCAPLUS RN Carbonic acid, magnesium salt (2:1) (8CI, 9CI) (CA INDEX NAME) CN 0 HO- C- OH 1/2 Mg L89 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2003 ACS ΑN 1991:30127 HCAPLUS DN 114:30127 Immunoactive compositions containing .gamma.-inulin and an antigen-binding TIΙN Cooper, Peter Dodd Australian National University, Australia PΑ SO PCT Int. Appl., 28 pp. CODEN: PIXXD2 DT Patent LΑ English IC ICM A61K039-39 CC 63-6 (Pharmaceuticals) Section cross-reference(s): 1, 15 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE _____ ______ ------____ _____ WO 9001949 19900308 19890817 PΙ A1 WO 1989-AU349 W: AU, JP, US RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE CA 1989-608534 19890816 CA 1337047 A1 19950919 AU 1989-41876 19890817 AU 8941876 Α1 19900323 19920213 AU 620149 В2 EP 1989-909684 19890817 EP 431023 19910612 Α1 19950405 EP 431023 В1 R: BE, CH, DE, FR, GB, IT, LI, NL T2 19920227 JP 1989-509078 19890817 JP 04501105

JP 3001214

US 5476844

WO 1989-AU349

PRAI AU 1988-9938

B2

Α Α

20000124 A 19951219

19880818

19890817

US 1991-656081

19910416

AB An immunotherapeutic compn. comprises inulin (I) or its derivs. in .gamma.-polymorphic form, an antigen-binding material, and optionally an immune modulator, such as an antigen or a cytokine. The antigen-binding material is a substance of low soly. capable of binding proteins, lipid, carbohydrates, and antigenic substances and selected from metal-contg. ppts., such as Al(OH)3 gels. The compn. is useful for the treatment of allergic disorders, immune deficiency, rheumatic diseases, and other disorders related to a dysfunction of the immune systems. A soln. contg. I was slurried with 1% by vol. of Al(OH)3 gel to give a I concn. >5.0% (wt./vol.) and the suspension was cooled to 5.degree. and recrystd. for several days and kept at 37.degree. for several days to transform to the .gamma.-configuration, then centrifuged, resuspended in water, heated for 1 h at 50-52.degree., and washed to 0 supernatant refractive index. The obtained compn. was mixed with saline contg. keyhole limpet hemocyanin and injected into mice; the antibody response was increased several-fold over that produced in mice injected in parallel with the same antigen adsorbed on Al(OH)3 gel or admixed with .gamma.-I, or adsorbed to Al(OH)3 gel and mixed with .gamma.-I. Also, the compn. carrying on adsorbed keyhole limpet hemocyanin given to mice showed specific serum antibody titers greater than those from Freund's incomplete adjuvant and comparable to those from Freund's complete adjuvant. STinulin alum antigen carrier immune stimulant ΙT Complement RL: BIOL (Biological study) (alternative pathway of, activation of, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier for) ΙT Immunoglobulins RL: BIOL (Biological study) (anti-idiotype, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier and) ΙT Immunomodulators Immunostimulants Microorganism Antigens Interferons Lymphokines and Cytokines RL: BIOL (Biological study) (immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier and) TΤ Immunodeficiency Rheumatism (treatment of, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier for) ΙT (.gamma.-inulin and antigen-binding material and antigen combinations for) ΙΤ Allergy inhibitors Anthelmintics Neoplasm inhibitors Parasiticides Protozoacides (.gamma.-inulin and antigen-binding material combinations) IΤ Immunostimulants (adjuvants, .gamma.-inulin and antigen-binding material combinations) IT Digestive tract Nervous system (disease, treatment of, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier for) ΙT Toxins RL: BIOL (Biological study)

(endo-, immunotherapeutic compns. contg. .gamma.-inulin and

antigen-binding carrier and) IT Lymphokines and Cytokines RL: BIOL (Biological study) (interleukin 2, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier and) IT Lymphokines and Cytokines RL: BIOL (Biological study) (interleukins, immunotherapeutic compns. contq. .gamma.-inulin and antigen-binding carrier and) IT Bactericides, Disinfectants, and Antiseptics Fungicides and Fungistats Virucides and Virustats (medical, .gamma.-inulin and antigen-binding material combinations) ΙT Glycopeptides RL: BIOL (Biological study) (muramic acid-contg., immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier and) IT Pharmaceutical dosage forms (nasal, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) ΙT Pharmaceutical dosage forms (ophthalmic, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) ΙT Pharmaceutical dosage forms (oral, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) IT Polysaccharides, esters RL: BIOL (Biological study) (phosphates, as antigen-binding carriers, immunostimulants contg. .gamma.-inulin and) TT Pharmaceutical dosage forms (rectal, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) IT Polysaccharides, esters RL: BIOL (Biological study) (sulfates, as antigen-binding carriers, immunostimulants contg. .gamma.-inulin and) ΙT Pharmaceutical dosage forms (topical, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) TT Lymphokines and Cytokines RL: BIOL (Biological study) (tumor necrosis factor, immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding carrier and) ΙT Pharmaceutical dosage forms (vaginal, .gamma.-inulin and antigen-binding carriers in, for immune response potentiation) ΙT 1305-62-0D, Calcium hydroxide, derivs. 1309-42-8D, Magnesium hydroxide, derivs. 1398-61-4, Chitin 7487-88-9D, Magnesium sulfate, derivs. 7778-18-7778-18-9D, Calcium sulfate, 9004-34-6D, Cellulose, 7784-30-7D, Aluminum phosphate, derivs. derivs. 9004-54-0, Dextran, biological studies 9005-49-6, Heparin, derivs. 9012-76-4, Deacetylchitin 10043-01-3D 10043-83-1D, Magnesium phosphate, derivs. 10043-01-3D, Aluminum biological studies sulfate, derivs. 10103-46-5D, Calcium phosphate, derivs. 21645-51-2D, Aluminum hydroxide, derivs. RL: BIOL (Biological study) (as antigen-binding carriers, immunostimulants contg. .gamma.-inulin and) ΙT 111069-91-1, Thymus-stimulating hormone

(immunotherapeutic compns. contg. .gamma.-inulin and antigen-binding

RL: BIOL (Biological study)

carrier and)

```
9005-80-5, Inulin
                         9005-80-5D, Inulin, esters and ethers
IT
                                                                  25702-76-5
     RL: BIOL (Biological study)
        (.gamma.-form of, immunostimulants contg. antigen-binding carrier and)
     1309-42-8D, Magnesium hydroxide, derivs.
IT
     RL: BIOL (Biological study)
        (as antigen-binding carriers, immunostimulants contg. .gamma.-inulin
        and)
     1309-42-8
RN
               HCAPLUS
     Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
CN
HO-Mg-OH
L89
     ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2003 ACS
     1990:558659 HCAPLUS
ΑN
DN
     113:158659
     Modification of aluminum hydroxide used as an adjuvant
TI
ΑU
     Stas, N. F.; Konovalova, Z. S.; Marchenko, N. A.
CS
     Tomsk. Politkeh. Inst., Tomsk, USSR
     Khimiko-Farmatsevticheskii Zhurnal (1990), 24(7), 65-6
SO
     CODEN: KHFZAN; ISSN: 0023-1134
DT
     Journal
LA
     Russian
CC
     63-8 (Pharmaceuticals)
AR
     Al(OH)3, a vaccine adjuvant, modified by Mg(
     OH) 2 showed enhanced activity (coeff. of sorption
     activity 710-720 \text{ mg} Congo red/1 g Al2O3). This effect may be useful in
     the prodn. of vaccines to reduce the dose of the
     adjuvant.
ST
     aluminum hydroxide vaccine adjuvant modification;
     magnesium hydroxide vaccine adjuvant
     modification
TΤ
     Vaccines
        (adjuvant, aluminum hydroxide modified by magnesium
        hydroxide as, sorption of)
     Adsorption
TΤ
        (by aluminum hydroxide modified by magnesium
        hydroxide, vaccines prepn. in relation to)
     1309-42-8, Magnesium hydroxide
TT
     RL: BIOL (Biological study)
        (aluminum hydroxide as vaccine adjuvant
        modification by, sorption in relation to)
     1310-73-2, Sodium hydroxide, biological studies
                                                        1336-21-6, Ammonium
TΤ
     hydroxide
     RL: BIOL (Biological study)
        (in aluminum hydroxide modification by magnesium
        hydroxide, sorption in relation to)
                                                         7786-30-3, Magnesium
TΤ
     7487-88-9, Magnesium sulfate, biological studies
     chloride, biological studies
                                    10377-60-3, Magnesium nitrate
     RL: BIOL (Biological study)
        (magnesium hydroxide prepn. from, for aluminum
        hydroxide modification, sorption in relation to)
     21645-51-2, Aluminum hydroxide, biological studies
TT
     RL: BIOL (Biological study)
        (vaccine adjuvant, modification by
        magnesium hydroxide of, sorption in relation to)
TΤ
     1309-42-8, Magnesium hydroxide
     RL: BIOL (Biological study)
        (aluminum hydroxide as vaccine adjuvant
        modification by, sorption in relation to)
     1309-42-8 HCAPLUS
RN
```

CN Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)

```
HO-Mg-OH
```

```
ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2003 ACS
L89
AN
    1982:550758 HCAPLUS
DN
    97:150758
    Injectable fat-protein emulsions and their use in therapy
TΤ
IN
    Glas, Bernard; Bacques, Claude Paul
PA
    Etablissements Gattefosse, Fr.
SO
    Fr. Demande, 9 pp.
    CODEN: FRXXBL
DT
    Patent
LA
    French
IC
    A61K037-02
    63-6 (Pharmaceuticals)
CC
FAN.CNT 1
    PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
                     ____
    -----
                                         -----
PΙ
    FR 2497668
                   A1
                           19820716
                                         FR 1981-635
                                                         19810115
    FR 2497668
                     B1 19860321
PRAI FR 1981-635
                           19810115
    Stable emulsions of fats and proteins for i.v. injection in
    treatment of nutritional disorders without affecting blood consts.
    contained proteins 55-65, NaHCO3 .apprx.2.26, triglycerides 6-40, and KCl
    0.4 g/L. The fats may be medium-chain triglycerides. An aq. emulsion
    which when subjected to autoclaving at 115.degree. for 20 min did not have
    appreciable fat hydrolysis was prepd. from acid casein 60, NaHCO3 2, KCl
    1.8, Mg(OH) 2 0.3, fats 6, and soybean
    lecithins 1 g/L, with the further addn. of sugars, vitamins, and trace
    elements.
ST
    casein glyceride emulsion parenteral
    Caseins, biological studies
ΙT
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (glyceride emulsions with, for parenteral nutrition)
TΤ
    Glycerides, compounds
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (C8-10-ethoxylated, casein-glyceride emulsions contg., for
       parenteral nutrition, Labrafac Hydro WL 1219)
TΤ
    Glycerides, biological studies
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (medium-chain, casein emulsions with, for parenteral
       nutrition)
ፐጥ
    Pharmaceuticals
        (parenterals, nutrient, casein-glyceride emulsions for)
TT
    144-55-8, biological studies 7447-40-7, biological studies
    RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (casein-glyceride emulsions contg., for parenteral nutrition)
```

=> sel hit rn

E10 THROUGH E18 ASSIGNED

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:13:27 ON 24 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 APR 2003 HIGHEST RN 504385-01-7 DICTIONARY FILE UPDATES: 23 APR 2003 HIGHEST RN 504385-01-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s e10-e18

1 546-93-0/BI (546-93-0/RN)1 1309-42-8/BI (1309-42-8/RN)1 26780-50-7/BI (26780-50-7/RN)1 34346-01-5/BI (34346-01-5/RN) 1 13463-67-7/BI (13463-67-7/RN)1 141256-04-4/BI (141256-04-4/RN) 1 172889-84-8/BI (172889-84-8/RN) 1 2090-64-4/BI (2090-64-4/RN)

1 66594-14-7/BI (66594-14-7/RN) L90 9 (546-93-0/BI OR 1

9 (546-93-0/BI OR 1309-42-8/BI OR 26780-50-7/BI OR 34346-01-5/BI OR 13463-67-7/BI OR 141256-04-4/BI OR 172889-84-8/BI OR 2090-64-4/BI OR 66594-14-7/BI)

=> d ide can tot

L90 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN **172889-84-8** REGISTRY

CN Sorbitan, tri-(9Z)-9-octadecenoate, mixt. with 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetr mono-(9Z)-9-octadecenoate poly(oxy-1,2-ethanedi INDEX NAME)

OTHER CA INDEX NAMES:

- CN 2,6,10,14,18,22-Tetracosahexaene, 2,6,10,15,19, (2E,6E,10E,14E,18E,22E)-, mixt. contg. (9CI)
- CN 2,6,10,14,18,22-Tetracosahexaene, 2,6,10,15,19,23-hexamethyl-, (all-E)-, mixt. contg.
- CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs., mixt. contg. (9CI)
- CN Sorbitan, mono-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs., (Z)-, mixt. contg.
- CN Sorbitan, tri-9-octadecenoate, (Z,Z,Z)-, mixt. with (all-E)-2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene and

Str references

```
foley - 09 / 925635
     (Z)-sorbitan mono-9-octadecenoate poly(oxy-1,2-ethanediyl) derivs.
OTHER NAMES:
     MF 59
CN
     MF 69
CN
     STEREOSEARCH
FS
DR
     172964-79-3
     C60 H110 O9 . C30 H50 . Unspecified
MF
CI
     MXS
SR
     CA
                BIOSIS, CA, CAPLUS, IPA, PHAR, TOXCENTER, USPATZ, USPATFULL
LC
     STN Files:
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          1
         9005-65-6
     CRN
     CMF
          Unspecified
     CCI
          PMS, MAN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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          2
     CRN 111-02-4
     CMF C30 H50
Double bond geometry as shown.
                                                            PAGE 1-A
                                                         Ме
                                            Ме
                                           E
                                                       Ε
Me<sub>2</sub>C
                                Е
                Мe
                            Me
                                                            PAGE 1-B
    .CMe2
     CM
          3
     CRN
         1333-71-7
     CMF
          C60 H110 O9
     CCI
          IDS
          CM
               4
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Double bond geometry as shown.

112-80-1

C18 H34 O2

CRN

CMF

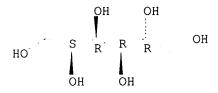
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 7 Z (CH_2) 7 Z

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CM 5

CRN 50-70-4

CMF C6 H14 O6
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Absolute stereochemistry.



49 REFERENCES IN FILE CA (1962 TO DATE) 49 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:88637 137:368575 REFERENCE 2: REFERENCE 3: 137:315844 137:293522 REFERENCE 4 . 137:246527 REFERENCE 5: 137:123752 REFERENCE 6:

REFERENCE 7: 137:62160

REFERENCE 8: 137:32060

REFERENCE 9: 136:293507

REFERENCE 10: 136:261424

L90 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN **141256-04-4** REGISTRY

CN .beta.-D-Glucopyranosiduronic acid, (3.beta.,4.alpha.,16.alpha.)-28-[[O-D-apio-.beta.-D-furanosyl-(1.fwdarw.3)-O-.beta.-D-xylopyranosyl-(1.fwdarw.4)-O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.2)-4-O-[5-[[5-(.alpha.-L-arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-1-oxooctyl]-6-deoxy-.beta.-D-galactopyranosyl]oxy]-16-hydroxy-23,28-dioxoolean-12-en-3-yl O-.beta.-D-galactopyranosyl-(1.fwdarw.2)-O-[.beta.-D-xylopyranosyl-(1.fwdarw.3)]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Oleanane, .beta.-D-glucopyranosiduronic acid deriv.

OTHER NAMES:

CN QA 21 CN QA 21V1

CN QS 21

CN Saponin QA 21V1

CN Stimulon

FS STEREOSEARCH

DR 170966-64-0, 154335-26-9

MF C92 H148 O46

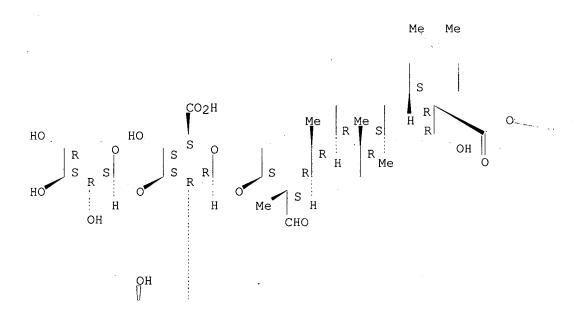
CI COM

SR CA

LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, DRUGNL, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-C

PAGE 2-A

__ OH

HO S R S O H

257 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

257 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:203660

REFERENCE 2: 138:185688

REFERENCE 3: 138:168809

REFERENCE 4: 138:121267

REFERENCE 5: 138:88646

REFERENCE 6: 138:88250

REFERENCE 7: 138:54096

REFERENCE 8: 138:37692

REFERENCE 9: 138:23654

REFERENCE 10: 138:23639

L90 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN **66594-14-7** REGISTRY

CN Quil-A (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Iscotec AB

CN Spikoside

ENTE A glycoside from Quillaja saponaria bark

```
MF
     Unspecified
     COM, MAN
CI
LC
     STN Files:
                  ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CANCERLIT, CAPLUS, CEN, CHEMLIST, CIN, EMBASE, IPA, MEDLINE, PROMT,
       RTECS*, TOXCENTER, USPAT2, USPATFULL
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             182 REFERENCES IN FILE CAPLUS (1962 TO DATE)
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            2:
                138:186392
REFERENCE
                138:121267
            3:
                138:112101
REFERENCE
            4:
REFERENCE
                138:105623
            5:
                138:54092
REFERENCE
            6:
REFERENCE
            7:
                138:37663
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            8 •
                137:368575
REFERENCE
            9:
                137:336553
REFERENCE 10: 137:316036
L90 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2003 ACS
     34346-01-5 REGISTRY
RN
     Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI)
                                                                          (CA
CN
     INDEX NAME)
OTHER CA INDEX NAMES:
    Acetic acid, hydroxy-, polymer with 2-hydroxypropanoic acid (9CI)
OTHER NAMES:
    (.+-.)-2-Hydroxypropanoic acid-hydroxyacetic acid copolymer
CN
CN
     Alzamer Depot
CN
     dl-Lactic acid-glycolic acid copolymer
CN
     DL-Lactic acid-glycolic acid copolymer
CN
     dl-Lactic acid-glycolic acid polymer
CN
     Glycolic acid-DL-lactic acid copolymer
CN
     Glycolic acid-lactic acid copolymer
CN
     Glycolic acid-lactic acid polymer
     Hydroxyacetic acid-(.+-.)-2-hydroxypropanoic acid copolymer
CN
CN
     Hydroxyacetic acid-2-hydroxypropionic acid copolymer
     Hydroxyacetic acid-lactic acid copolymer
CN
     Lactic acid-glycolic acid copolymer
CN
     Lactic acid-glycolic acid polymer
CN
CN
     PLGA 5010
CN
     PLGA 5020
CN
     Poly(DL-lactic acid-glycolic acid)
CN
     Poly(glycolic acid-co-DL-lactic acid)
CN
     Poly(glycolic acid-lactic acid)
CN
     Poly(lactic acid-glycolic acid)
CN
     Resolut
CN
     Resolut LT
CN
     Resolut ST
CN
     Resomer RG 502
```

CN

Resomer RG 502H

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CN
     Resomer RG 504H
     Resomer RG 858
CN
     RG 502H
CN
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MF
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CI
     Polyester, Polyester formed
PCT
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     CRN 50-21-5
     CMF C3 H6 O3
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REFERENCE
            9:
               138:242962
REFERENCE 10: 138:226719
L90 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN
     26780-50-7 REGISTRY
     1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione
```

(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

```
1,4-Dioxane-2,5-dione, polymer with 3,6-dimethyl-1,4-dioxane-2,5-dione
CN
     (9CI)
     p-Dioxane-2,5-dione, 3,6-dimethyl-, polyester with p-dioxane-2,5-dione
CN
    p-Dioxane-2,5-dione, polyester with 3,6-dimethyl-p-dioxane-2,5-dione (8CI)
CN
OTHER NAMES:
     1,4-Dioxane-2,5-dione-1-DL-3,6-dimethyl-1,4-dioxane-2,5-dione copolymer
CN
     3,6-Dimethyl-1,4-dioxane-2,5-dione-1,4-dioxane-2,5-dione copolymer
CN
CN
CN
     Diglycolide-DL-dilactide copolymer
CN
     DL-Lactide-glycolide copolymer
CN
     Ethicon W 9045
     Glycolide-dl-lactide copolymer
CN
CN
     Glycolide-DL-lactide copolymer
CN
     Glycolide-DL-lactide polymer
CN
     Glycolide-lactide copolymer
CN
     Glycolide-lactide polymer
CN
     Lactide-diglycolide copolymer
CN
    Lactide-glycolide copolymer
CN
    Medisorb
    Medisorb (polymer)
CN
CN
    Medisorb 5050DL
CN
    Medisorb 8515DL
CN
     PLG
CN
     Poly(dl-lactide-co-glycolide)
CN
     Poly(DL-lactide-glycolide)
CN
     Poly(glycolide-co-lactide)
CN
     Poly(glycolide-lactide)
CN
     Poly(lactide-co-glycolide)
CN
     Poly-(DL)-lactide-co-glycolide
CN
     Polyglactin
CN
     Polyglactin 370
CN
     Polyglactin 910
CN
     Resomer R 6-503
CN
     Resomer RG 206
CN
     Resomer RG 501H
CN
     Resomer RG 503
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    Resomer RG 504
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     Resomer RG 505
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     Resomer RG 506
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     Resomer RG 756
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    RG 501H
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    RG 503
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     RG 503H
CN
     RG 504
     RG 755
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CN
     Vicryl
     Vicryl 910
CN
CN
     Vicryl PM
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     460731-87-7
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     PMS, COM
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PCT
     Polyester, Polyester formed
                ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
LC
     STN Files:
       CA, CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE,
       IFICDB, IFIPAT, IFIUDB, IPA, NIOSHTIC, PIRA, PROMT, TOXCENTER, USAN,
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USPAT2, USPATFULL

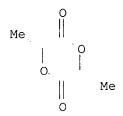
CM 1

CRN 502-97-6 CMF C4 H4 O4

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CM 2

CRN 95-96-5 CMF C6 H8 O4



2097 REFERENCES IN FILE CA (1962 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2112 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:260484

REFERENCE 2: 138:260470

REFERENCE 3: 138:260458

REFERENCE 4: 138:260411

REFERENCE 5: 138:260341

REFERENCE 6: 138:260340

REFERENCE 7: 138:260263

REFERENCE 8: 138:260247

REFERENCE 9: 138:260229

REFERENCE 10: 138:255738

L90 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN 13463-67-7 REGISTRY

CN Titanium oxide (TiO2) (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1385RN59

CN 1500D

CN 234DA

CN 500HD

```
63B1 White
CN
CN
     A 100
CN
     A 160
CN
     A 200
CN
     A 200 (pigment)
CN
     A 330
CN
     A 330 (pigment)
CN
     A-Fil Cream
CN
     A-FN 3
CN
     Aerolyst 7710
CN
     Aerosil P 25
CN
     Aerosil P 25S6
CN
     Aerosil P 27
CN
     AF-E 3D
CN
     AK 15
CN
     AK 15 (pigment)
CN
     AM 100
CN
     Amperit 780.0
CN
     AMT 100
CN
     AMT 600
     AUF 0015S
CN
CN
     Austiox R-CR 3
CN
     B 101
CN
     B 101 (pigment)
CN
     Bayer R-FD 1
CN
     Bayertitan A
CN
     Bayertitan AN 3
CN
     Bayertitan R-FD 1
CN
     Bayertitan R-FK 21
CN
     Bayertitan R-FK-D
CN
     Bayertitan R-KB 2
CN
     Bayertitan R-KB 3
CN
     Bayertitan R-KB 4
CN
     Bayertitan R-KB 5
CN
     Bayertitan R-KB 6
CN
     Bayertitan R-U 2
CN
     Bayertitan R-U-F
CN
     Bayertitan R-V-SE 20
CN
     Bayertitan T
     Bistrater L-NSC 200C
CN
CN
     BR 29-7-2
     C 97
CN
     C 97 (oxide)
CN
CN
     C.I. 77891
     C.I. Pigment White 6
CN
CN
     Cab-O-Ti
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
     DISPLAY
     51745-87-0
AR
     494848-07-6, 494848-23-6, 494851-77-3, 494851-98-8, 12000-59-8,
DR
     12701-76-7, 12767-65-6, 12789-63-8, 1309-63-3, 1344-29-2, 55068-84-3,
     55068-85-4, 62338-64-1, 101239-53-6, 98084-96-9, 37230-92-5, 37230-94-7, 37230-95-8, 37230-96-9, 39320-58-6, 39360-64-0, 39379-02-7, 100292-32-8,
     116788-85-3, 185323-71-1, 185828-91-5, 188357-76-8, 188357-79-1,
     195740-11-5, 221548-98-7, 224963-00-2, 246178-32-5, 252962-41-7
     02 Ti
ΜF
CI
     COM
LC
                   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS,
     STN Files:
       BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
       DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT,
       ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA,
```

ULIDAT, USAN, USPAT2, USPATFULL, VTB
 (*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
 (**Enter CHEMLIST File for up-to-date regulatory information)

O== Ti== O

111072 REFERENCES IN FILE CA (1962 TO DATE)
1528 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
111320 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:264907

REFERENCE 2: 138:264881

REFERENCE 3: 138:264879

REFERENCE 4: 138:264871

REFERENCE 5: 138:264804

REFERENCE 6: 138:264605

REFERENCE 7: 138:264348

REFERENCE 8: 138:264336

REFERENCE 9: 138:264257

REFERENCE 10: 138:264217

L90 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN **2090-64-4** REGISTRY

CN Carbonic acid, magnesium salt (2:1) (8CI, 9CI) (CA INDEX NAME) OTHER NAMES:

CN Magnesium bicarbonate

CN Magnesium bicarbonate (Mg(HCO3)2)

CN Magnesium hydrogen carbonate

MF C H2 O3 . 1/2 Mg

CI COM

LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CHEMLIST, CIN, DETHERM*, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, PDLCOM*, PROMT, TOXCENTER, TULSA, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

CRN (463-79-6)

но— с— он

1/2 Mg

393 REFERENCES IN FILE CA (1962 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

393 REFERENCES IN FILE CAPLUS (1962 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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REFERENCE
            1: 138:240043
               138:124777
REFERENCE
            2:
REFERENCE
                138:124248
            3:
REFERENCE
            4:
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REFERENCE
            6:
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                137:252664
REFERENCE
            7:
                137:237456
REFERENCE
            8:
                137:204193
REFERENCE
            9:
REFERENCE 10: 137:172175
L90 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN
    1309-42-8 REGISTRY
    Magnesium hydroxide (Mg(OH)2) (9CI) (CA INDEX NAME)
CN
OTHER NAMES:
CN
    10A
CN
     10A (hydroxide)
    200-06H
CN
CN
    Alcanex NHC 25
    Asahi Glass 200-06
CN
    Combustrol 500
CN
    Daimushew 6000
CN
    DP 393
CN
CN
    DSB 100
CN
    Duhor
    Duhor N
CN
    Ebson RF
CN
    Finemag MO-T
CN
    Finemag SN-L
CN
CN
    FloMag H
    FloMag HUS
CN
    FR 20
CN
    FR 20-310-
CN
CN
    Hydrofy G 1.5
CN
    Hydrofy G 2.5
CN
    Hydrofy N
CN
    Ki 22-5B
    Kisma KX 4SU
CN
    Kisuma
CN
    Kisuma 120
CN
    Kisuma 2
CN
CN
    Kisuma 3A
CN
    Kisuma 4AF
    Kisuma 5
CN
CN
    Kisuma 54A
CN
    Kisuma 5A
CN
    Kisuma 5A-N
CN
    Kisuma 5AU
CN
    Kisuma 5B
CN
    Kisuma 5B-N
CN
     Kisuma 5BG
CN
    Kisuma 5E
```

```
Kisuma 5EU
CN
CN
     Kisuma 5J
     Kisuma 5P
CN
     Kisuma 6E
CN
     Kisuma 7B
CN
CN
     Kisuma KX 4SU
CN
     Kisuma S 4
     KX 4S
CN
     KX 80
CN
     KX 8S(A)
CN
CN
     KX 8S(B)
CN
     Kyowamag F
CN
     Lederscon
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
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     12195-86-7, 13760-51-5
DR
MF
     H2 Mg O2
CI
     COM
                  ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
LC
     STN Files:
       CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,
       CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT,
       ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
       MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*,
       TOXCENTER, TULSA, USAN, USPAT2, USPATFULL, VETU, VTB
         (*File contains numerically searchable property data)
                      DSL**, EINECS**, TSCA**
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
HO-Mq-OH
           11581 REFERENCES IN FILE CA (1962 TO DATE)
             156 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           11603 REFERENCES IN FILE CAPLUS (1962 TO DATE)
               1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
REFERENCE
            1: 138:264859
                138:260473
REFERENCE
            2:
                138:260445
REFERENCE
            3:
REFERENCE
            4:
                138:260109
                138:260101
REFERENCE
            5:
                138:260021
REFERENCE
            6:
                138:259449
REFERENCE
            7:
REFERENCE
            8:
                138:259044
                138:256332
REFERENCE
            9:
REFERENCE 10: 138:256210
L90 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2003 ACS
     546-93-0 REGISTRY
     Carbonic acid, magnesium salt (1:1) (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Magnesium carbonate (6CI, 7CI)
OTHER NAMES:
```

```
CN
    Apolda
CN
    C.I. 77713
    Carbonate magnesium
CN
     DCI Light Magnesium Carbonate
CN
CN
CN
     Gold Star
     Gold Star (carbonate)
CN
    GP 20
CN
    GP 20 (carbonate)
CN
    GP 30
CN
CN
    GP 30 (carbonate)
CN
    Kimboshi
CN
    MA 70 (carbonate)
CN
    Magfy
CN
    Magnesium carbonate (1:1)
    Magnesium carbonate (MgCO3)
CN
CN
     Stan-Mag Magnesium Carbonate
     7757-69-9
AR
     1784-39-0, 183480-27-5, 364320-47-8
DR
    C H2 O3 . Mg
ΜF
CI
    COM
                  ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
LC
     STN Files:
       CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGU,
       EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NAPRALERT, NIOSHTIC,
       PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USAN, USPAT2, USPATFULL,
       VETU, VTB
         (*File contains numerically searchable property data)
                     DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN
     (463 - 79 - 6)
   0
HO-C-OH
   Ma
            6851 REFERENCES IN FILE CA (1962 TO DATE)
             114 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            6863 REFERENCES IN FILE CAPLUS (1962 TO DATE)
              19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
REFERENCE
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REFERENCE
            2:
REFERENCE
            3:
                138:259044
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7: 138:241717 REFERENCE 8: 138:240362 REFERENCE

4:

5:

6:

138:243990

138:243332

138:242911

REFERENCE

REFERENCE

REFERENCE

REFERENCE 9: 138:240046

REFERENCE 10: 138:240045

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L8 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2003 ACS

RN 76110-00-4 REGISTRY

CN Carbonic acid, magnesium salt (9:5), monohydrate (9CI) (CA INDEX NAME)

MF C H2 O3 . 1/9 H2 O . 5/9 Mg

LC STN Files: GMELIN*

(*File contains numerically searchable property data)

CRN (463-79-6)

О || НО— С— ОН

5/9 Mg

1/9 H₂O

L8 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2003 ACS

RN 68973-26-2 REGISTRY

CN Carbonic acid, magnesium salt (1:1), dihydrate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Magnesium carbonate (MgCO3) dihydrate

MF C H2 O3 . 2 H2 O . Mg

LC STN Files: CA, CAPLUS, GMELIN*

(*File contains numerically searchable property data)

CRN (463-79-6)

Mg

2 H₂O

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 90:62102

L8 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2003 ACS

```
61042-72-6 REGISTRY
RN
     Carbonic acid, magnesium salt (1:1), pentahydrate (9CI) (CA INDEX NAME)
CN
OTHER NAMES:
     Magnesium carbonate (MgCO3) pentahydrate
CN
     Magnesium carbonate pentahydrate
CN
     C H2 O3 . 5 H2 O . Mg
MF
                  AGRICOLA, BIOSIS, CA, CAPLUS, GMELIN*, TOXCENTER
LC
     STN Files:
         (*File contains numerically searchable property data)
CRN
    (463 - 79 - 6)
   0
HO-C-OH
    Mq
 5 H<sub>2</sub>O
              14 REFERENCES IN FILE CA (1962 TO DATE)
              14 REFERENCES IN FILE CAPLUS (1962 TO DATE)
            1: 136:219810
REFERENCE
REFERENCE
               135:51120
            2:
REFERENCE
            3:
                129:179332
                129:56582
REFERENCE
            4:
REFERENCE
            5:
                123:235681
                115:20830
REFERENCE
            6:
REFERENCE
            7:
                112:237644
REFERENCE
            8:
                111:181933
                104:228808
REFERENCE
            9:
REFERENCE 10: 104:71115
     ANSWER 4 OF 8 REGISTRY COPYRIGHT 2003 ACS
Г8
RN
     33660-53-6 REGISTRY
     Carbonic acid, magnesium salt (1:1), tetrahydrate (8CI, 9CI) (CA INDEX
CN
     NAME)
OTHER NAMES:
     Magnesium carbonate (MgCO3) tetrahydrate
CN
     C H2 O3 . 4 H2 O . Mg
STN Files: CA, CAPLUS, GMELIN*
ΜF
LC
         (*File contains numerically searchable property data)
CRN
    (463 - 79 - 6)
```

Mg

4 H₂O

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 90:62102

REFERENCE 2: 75:53782

L8 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2003 ACS

RN 23389-33-5 REGISTRY

CN Carbonic acid, magnesium salt (1:1), hydrate (8CI, 9CI) (CA INDEX NAME) OTHER NAMES:

CN Magnesium carbonate hydrate

MF C H2 O3 . \mathbf{x} H2 O . Mg

LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM, GMELIN*, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, TOXCENTER, USAN, USPATFULL

(*File contains numerically searchable property data) CRN (463-79-6)

Mg

x H₂O

18 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

18 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:313174

REFERENCE 2: 129:217390

REFERENCE 3: 128:103226

REFERENCE 4: 124:119612

REFERENCE 5: 123:148293

REFERENCE 6: 123:12338

REFERENCE

7: 115:282932

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REFERENCE
           8: 111:118268
               104:23314
REFERENCE
          9:
REFERENCE 10: 98:88299
     ANSWER 6 OF 8 REGISTRY COPYRIGHT 2003 ACS
^{18}
RN
     17968-26-2 REGISTRY
CN
     Carbonic acid, magnesium salt (1:1), monohydrate (8CI, 9CI) (CA INDEX
     NAME)
OTHER NAMES:
    Magnesium carbonate (MgCO3) monohydrate
CN
MF
     C H2 O3 . H2 O . Mg
                  CA, CAPLUS, GMELIN*
LC
     STN Files:
         (*File contains numerically searchable property data)
CRN (463-79-6)
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HO- C- OH
    Mg
   H20
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               8 REFERENCES IN FILE CAPLUS (1962 TO DATE)
REFERENCE
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               90:62102
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            3:
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REFERENCE
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               71:27017
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            5:
               70:32912
REFERENCE
            6:
               69:28939
REFERENCE
            7:
               68:70743
REFERENCE
            8: 67:120408
     ANSWER 7 OF 8 REGISTRY COPYRIGHT 2003 ACS
L8
     14481-62-0 REGISTRY
RN
     Carbonic acid, magnesium salt, hydrate (8CI) (CA INDEX NAME)
CN
MF
     C H2 O3 . \mathbf{x} H2 O . \mathbf{x} Mg
LC
     STN Files:
                  GMELIN*
         (*File contains numerically searchable property data)
CRN
    (463 - 79 - 6)
```

x Mg

x H₂O

```
ANSWER 8 OF 8 REGISTRY COPYRIGHT 2003 ACS
\Gamma8
RN
     5145-46-0 REGISTRY
     Carbonic acid, magnesium salt (1:1), trihydrate (8CI, 9CI) (CA INDEX
CN
     NAME)
OTHER NAMES:
     Magnesium carbonate (MgCO3) trihydrate
CN
CN
     Magnesium carbonate trihydrate
     C H2 O3 . 3 H2 O . Mg
MF
                  AGRICOLA, BIOSIS, CA, CAOLD, CAPLUS, GMELIN*, TOXCENTER,
LC
     STN Files:
         (*File contains numerically searchable property data)
CRN
    (463 - 79 - 6)
```

Mg

3 H₂O

- 97 REFERENCES IN FILE CA (1962 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 97 REFERENCES IN FILE CAPLUS (1962 TO DATE)
 3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
- REFERENCE 1: 136:219810
 REFERENCE 2: 136:218014
 REFERENCE 3: 135:378823
 REFERENCE 4: 135:51120
 REFERENCE 5: 130:305482
- REFERENCE 5: 130:305482
- REFERENCE 6: 130:155697
- REFERENCE 7: 129:321843
- REFERENCE 8: 129:56582

REFERENCE 9: 126:64146

REFERENCE 10: 126:26021

=> fil wpix

FILE 'WPIX' ENTERED AT 16:25:28 ON 24 APR 2003 COPYRIGHT (C) 2003 THOMSON DERWENT

FILE LAST UPDATED: 10 APR 2003 <20030410/UP>
MOST RECENT DERWENT UPDATE: 200324 <200324/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

Due to data production problems the WPI file had to be reset to update 200323. SDIs for update 24 will be rerun free of charge once the corrected data is loaded. Also answer sets created after April 10 may at least temporarily be affected and hence partially invalid.

- >>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<
- >>> SLART (Simultaneous Left and Right Truncation) is now
 available in the /ABEX field. An additional search field
 /BIX is also provided which comprises both /BI and /ABEX <<</pre>
- >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
- >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
 SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<
- >>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
 PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

- >>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
 GUIDES, PLEASE VISIT:
 http://www.derwent.com/userguides/dwpi guide.html <<<</pre>
- => d all abeq tech abex tot
- L118 ANSWER 1 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 2003-229201 [22] WPIX

DNC C2003-058769

- TI Immunological adjuvant composition comprising lipid phase and gel obtained by complexing polyvalent metal cation with anionic polymer, providing vaccines with good initial and long-term effectiveness.
- DC A96 B04 D16
- IN DUPUIS, L; TROUVE, G
- PA (SEPP) SEPPIC SOC EXPL PROD IND CHIM

CYC 21

- PI WO 2002080840 A2 20021017 (200322)* FR 23p A61K000-00 <-RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
 W: JP US
 - FR 2823119 A1 20021011 (200322) A61K047-44 <--

ADT WO 2002080840 A2 WO 2002-FR1057 20020327; FR 2823119 A1 FR 2001-4644 20010405

PRAI FR 2001-4644 20010405

- IC ICM A61K000-00; A61K047-44
 ICS A61K039-00
- ICI A61K047-44, A61K047:06, A61K047:30

AB WO 200280840 A UPAB: 20030402

NOVELTY - A new composition (I) comprises:

- (a) a lipid phase; and
- (b) an organometallic gel obtained by complexation of polyvalent metal cation(s) with anionic polymer(s).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of (I).

USE - The use of (I) is claimed as adjuvant phase in a vaccine composition, the claims also cover the production of a vaccine using (I) as immunological adjuvant and a composition comprising at least one antigen (or compound inducing formation of a specific amino acid sequence in vivo) and (I) (claimed). (I) is especially useful for improving the immune response to viral, bacterial or parasitic antigens (e.g. rabies, Aujeszky's disease or foot and mouth disease virus, HIV, Escherichia coli, Pasteurella, Staphylococcus, Streptococcus, Trypanosoma, Plasmodium or Leishmania antigens), but may also be used with e.g. nucleic acid-based or anticancer vaccines.

ADVANTAGE - Vaccines containing (I) as adjuvant provide both a rapid onset of protection and a long-lasting protective effect against diseases.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A10-E21B; A12-V01; B04-B01B; B04-B01C; B04-B04C; B04-C02; B04-C02C; B04-C03; B05-A01B; B05-A03A; B05-B01P; B05-C04; B05-C08; B07-A02A; B07-A02B; B10-A07; B10-C02; B10-C04B; B10-C04E; B10-E04C; B10-G02; B14-S11; D05-H07

TECH UPTX: 20030402

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Lipids: The lipid phase (a) comprises one or more of animal, vegetable or mineral oils (specifically bleached mineral, peanut, olive, sesame, soya, wheat-germ, grape seed, sunflower, castor, linseed, copra, palm, walnut, hazelnut or rape oil, olive squalane or squalene or fish liver extract), alkyl (specifically 1-4C alkyl) esters of these oils, fatty acid alkyl esters (specifically esters of 12-22C fatty acids, preferably myristate, palmitate, oleate, rincoleate or isostearate esters, especially ethyl oleate, methyl oleate, isopropyl myristate or octyl palmitate), fatty acid esters of polyols (specifically mono-, di- or triglycerides or esters of polyglycerol, propylene glycol, hexols (especially sorbitol or mannitol) or anhydro-hexols (especially sorbitan or mannitan)) or fatty alcohol ethers of polyols.

Preferred Composition: (I) is an emulsion, preferably containing the lipid phase (a) at 5-70 (preferably 15-60) wt. % as the continuous phase (in which the gel (b) is dispersed). (I) optionally also contains surfactant(s), specifically nonionic surfactants selected from polyglycerol esters sugar esters (e.g. sorbitan, mannitan or sucrose esters), ethoxylated sugars, ethoxylated fatty acids or esters, mono- or diglycerides modified by reaction with acetic or lactic acid, ethoxylated mono-, di- or triglycerides or sugar ethers (e.g. glucose, xylose or lactitol ethers). The surfactant (or surfactant mixture) specifically has HLB 4-12 (especially 5-8); and is contained in (I) at 0.5-10 (preferably 1-5) wt. %.

Preparation: Claimed preparation of (I) involves:

- (i) preparing an aqueous solution or suspension containing insoluble polyvalent cation salt(s), soluble anionic polymer(s) and optionally hydrophilic surfactant(s);
- (ii) emulsifying the obtained suspension with an oil phase, optionally containing lipophilic surfactant;
- (\mbox{iii}) if necessary solubilizing the salt by adjusting the pH of the emulsion;
- (iv) optionally adding an excess of the cation; and
- (v) neutralizing the emulsion. In a variant the obtained emulsion is

dissolved in a solvent for the lipid phase to give a suspension of the gel, which is centrifuged to isolate the gel.

TECHNOLOGY FOCUS - POLYMERS - Preferred Gels: The gels (b) are obtained by mixing appropriate amounts of a solution or suspension of the cation(s) (preferably di- or trivalent cations, especially calcium, magnesium, zinc, trivalent iron or aluminum) and a solution or suspension of the polymer(s) (preferably sulfated polymer, dextran, carrageenate, carboxylated polymer, polyacrylate, pectin, alginate, natural gum, xanthan gum or guar gum, especially sodium alginate), optionally under stirring, preferably in an aqueous medium. The cation is specifically used as 0.001-10 (preferably 0.1-1) M solution or suspension of the hydroxide, carbonate, citrate, gluconate, glucoheptonate, fructoheptonate, lactate, acetate, salicylate or glycerophosphate salt. The salt is especially calcium hydroxide, magnesium carbonate, manganese carbonate, calcium gluconate, manganese gluconate, manganese glycerophosphate, zinc qluconate, calcium fructoheptonate, aluminum salicylate or aluminum acetate, particularly manganese glycerophosphate (optionally mixed with manganese gluconate). The cation is specifically used as 0.1-10(preferably 1-5) wt. % solution or suspension.

ABEX

UPTX: 20030402 EXAMPLE - A 3.5% solution of Saltialgine S80 (RTM; low viscosity sodium alginate with high guluronic acid content) and a 500 microM suspension of manganese glycerophosphate were prepared. A mixture of 1 ml of the suspension, 20 ml of the solution and 1.05 g Montanox 80 (RTM; polyoxyethylene (80) sorbitan oleate; HLB 15) was dispersed in 100 g of Marcol 52 (RTM; bleached mineral oil) containing 5 weight % Montane 80 (RTM; sorbitan monooleate; HLB 4.3) under stirring at 3000 rpm for 3 minutes, the overall HLB of the surfactant system being 6. The obtained emulsion was neutralized with a few drops of concentrated acetic acid (to solubilize the manganese glycerophosphate and form manganese alginate complex) then neutralized to pH 5.5 with sodium hydroxide, giving an adjuvant emulsion (Ia) consisting of a continuous oil phase and dispersed manganese alginate gel. The effectiveness of (Ia) was tested in mice, using vaccines containing ovalbumin as antigen and (Ia) as adjuvant. A combination of equal amounts of vaccine and adjuvant gave IgG1 titers of 64000, 64000 and 96000 after 28, 56 and 90 days respectively and IgG2a titers of 2400, 16000 and 24000 after 28, 56 and 90 days respectively. For comparison, the antigen alone gave both IgG1 and IgG2a titers of 100, 1000 and 100 after 28, 56 and 90 days respectively.

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L118 ANSWER 2 OF 14 WPIX (C) 2003 THOMSON DERWENT
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AN 2002-698585 [75] WPIX

DNC C2002-197797

TI Composition for controlled release injections using soluble glass microspheres suspended in anhydrous liquid.

DC A96 B07

IN ROSER, B J; ROSER, B

PA (ROSE-I) ROSER B J; (CAMB-N) CAMBRIDGE BIOSTABILITY LTD; (IDEA-N) IDEA INC

PI WO 2002066005 A1 20020829 (200275)* EN 23p A61K009-00 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

US 2002155129 A1 20021024 (200277) A61K039-12

ADT WO 2002066005 A1 WO 2002-US4269 20020214; US 2002155129 A1 US 2001-784153 20010216

PRAI US 2001-784153 20010216

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ICM A61K009-00; A61K039-12
IC
     ICS A61K009-14; A61K009-16; A61K039-02
     WO 200266005 A UPAB: 20021120
AB
     NOVELTY - A composition for controlled release injections
     comprises soluble glass microspheres containing a drug or vaccine
      suspended in anhydrous liquid.
          DETAILED DESCRIPTION - An injectable composition comprises
     a stabilized drug or vaccine in soluble glass microspheres,
     suspended in an anhydrous liquid, where the drug or vaccine is
     protected against dissolution while surrounded by anhydrous liquid,
     extending the duration of action of the drug or the triggering of the
     immune response by the vaccine, long after injection
     by slowly releasing the drug or vaccine.
          An INDEPENDENT CLAIM is included for a method of formulating a drug
     or vaccine to prolong the duration of action, by incorporating
     the drug or vaccine in soluble glass microspheres, and
     suspending the microspheres in an anhydrous liquid.
          USE - This method of delivery is for the administration of drugs and
     vaccines.
     Dwg.0/2
FS
     CPI
FΑ
     AB; DCN
     CPI: A12-V01; B04-B01B; B04-B04M; B04-C02; B04-C03D; B04-D01; B04-E01;
MC
          B04-F06; B04-F10; B04-F11; B04-N04; B04-N05; B05-A01B; B05-A03;
          B05-B01B; B05-B02A; B05-B02A3; B05-C07; B05-C08; B07-A02B; B10-A07;
          B10-H02B; B12-M03; B12-M10A; B12-M11E; B12-M11G; B14-A01; B14-C01;
          B14-C03; B14-D01; B14-F01; B14-F02; B14-F04; B14-F08; B14-G02;
          B14-G03; B14-H01B; B14-J01; B14-P01; B14-S11
                    UPTX: 20021120
TECH
     TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Drugs: The drug is a
     hormone, analgesic, narcotic, narcotic antagonist, chemotherapeutic,
     immunosuppressant, growth or differentiation regulator or factor,
     immunomodulator, contraceptive, vasoactive agent, coagulation modifier,
     cardioactive, antiinflammatory or CNS drug. The vaccine is
     selected from toxins, toxoids, live or killed bacteria, live or killed
     viruses, live or killed protozoa, recombinant proteins, DNA, RNA,
     polysaccharides, lipoproteins and lipids and recombinant or synthetic
     peptides, particularly tetanus toxoid. The vaccine may be
     adsorbed to an adjuvant such as aluminium hydroxide, aluminium
     phosphate or calcium phosphate.
     Preferred Composition: The glass microspheres contain an amount of an
     insoluble biocompatible high-density agent (including calcium phosphate,
     aluminium phosphate, aluminium hydroxide, barium sulfate or
     titanium dioxide) sufficient to raise the average
     density of the microspheres to match that of the anhydrous liquid in which
     they are suspended.
     TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Microspheres: The
     microspheres comprise non-reducing sugars (such as sucrose, trehalose,
     raffinose or stachyose) and sugar alcohols (such as mannitol, arabinitol,
     inositol, glucitol, galactitol, xylitol, maltitol, lactitol,
     glucopyranosyl sorbitol or glucopyranosyl mannitol), metal carboxylates
     and phosphate glasses. They may be produced by spray-drying, air drying,
     vacuum drying, emulsion solidification, precipitation or melting and
     grinding to a fine powder.
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Preferred Liquids: The liquid is an anhydrous hydrophilic or hydrophobic liquid, anhydrous silicone fluid or anhydrous perfluorocarbon such as perfluorohexane, perfluorodecalin, perfluorooctane or perfluorophenanthrene.

ABEX UPTX: 20021120

ADMINISTRATION - The administration is by injection. EXAMPLE - Groups of 10 guinea pigs were injected with: (A) fresh liquid vaccine;

- (B) vaccine dried into a powder of sugar glass microspheres and rehydrated with water immediately before injection;
- (C) vaccine dried into a powder of sugar glass microspheres suspended in 0.5 ml squalane oil;
- (D) vaccine dried into a powder of sugar glass microspheres suspended in 0.5 ml perfluorodecalin; or
- (E) a powder of sugar glass microspheres not containing vaccine suspended in 0.5 ml perfluorodecalin.

The antibody titre in groups (A) and (B) fell at 12 weeks after injection. The titre in groups (C) and (D) did not fall at 12 weeks. There was no antibody response in groups (A) or (E).

L118 ANSWER 3 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 2002-619200 [66] WPIX

DNC C2002-174954

TI Method of enhancing the immune response of a patient relative to the normal immune response involves converting aspartic acid residue or asparigine residue to isoaspartic acid residue.

DC B04 D16

IN MAMULA, M J

PA (UYYA) UNIV YALE

CYC 99

PI WO 2002060390 A2 20020808 (200266)* EN 28p A61K000-00 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

ADT WO 2002060390 A2 WO 2002-US336 20020104

PRAI US 2001-259765P 20010104

IC ICM A61K000-00

AB WO 200260390 A UPAB: 20021014

NOVELTY - Enhancing the immune response of a patient relative to the normal immune response (M1) involves: converting aspartic acid residue or asparigine residue present in tumor antigen, bacterial protein or viral protein (A) while growing cells containing (A) to isoaspartic acid residue for producing an isoaspartic acid containing (A) and administering it to the patient.

DETAILED DESCRIPTION - Enhancing the immune response of a patient relative to the normal immune response (M1) involves: converting aspartic acid residue or asparigine residue present in tumor antigen, bacterial protein or viral protein (A) while growing cells containing (A) to isoaspartic acid residue for producing an isoaspartic acid containing (A) and administering it to the patient.

(M1) involves:

- (a) either growing cells containing a tumor antigen, bacterial protein or viral protein under conditions; and converting an aspartic acid residue (a) or an asparigine residue (b) in the tumor antigen, bacterial or viral protein to isoaspartic acid residue (c) for producing isoaspartic acid-containing tumor antigen, bacterial or viral protein (I);
 - (b) optionally isolating (I); and
- (c) administering (I) to the cells of a patient to enhance the immune response of the patient; or The method involves treatment of the tumor antigen, bacterial protein, or viral protein or its fragment to convert (a) or (b) to produce (I) and administering (I) to elicit the enhanced immune response.

INDEPENDENT CLAIMS are included for the following:

(1) enhancing the immune response of a patient relative to the normal immune response (M2) involving: administration of a peptide comprising 9-40 amino acid residues of a tumor antigen, bacterial protein or viral protein to the patient. The peptide comprises (a) or (b) that has been replaced by (c);

- (2) a vaccine (II) comprising a protein or its fragment containing (c) and a carrier. The protein is tumor antigens, bacterial proteins and/or viral proteins; and
 - (3) an antibody (III) reactive with the protein or its fragments. ACTIVITY Antibacterial; Virucide; Antitumor.

MECHANISM OF ACTION - Vaccine; Inhibitor; Stimulator of the immune response.

Test details are described but no specific results are given.

USE - (M1) is useful for enhancing the immune response of a patient relative to the normal immune response; as vaccine or antibody (claimed); for treating solid tumor masses (e.g. carcinomas and sarcomas), murine B16 melanoma, P815 murine mastocytoma, PTAS murine mammary carcinoma, colon rectal carcinoma, adenocarcinoma, glioblastoma multiform and astrosarcoma, cervical carcinoma, lung carcinomas, lymphomas (Hodgkin's and non-Hodgkin's), fibrosarcoma, myeloma); for treating bacteria such as Bacillus anthracus, Mycobacterium, Streptococcus, Staphylococcus, Neisseria, Chlamydia, Haemophilus, Borrelia burgdorferi; for treating virus e.g. Hepatitis A, Hepatitis B, Hepatitis C, Rabies, HIV, influenza, Measles, Rotavirus, Herpes simplex virus.

ADVANTAGE - The method enhances the immune response of a patient relative to the normal immune response; identifies the weakly antigenic proteins found on tumors, bacterias and viruses. The method provides vaccine and antibody, which selects and eliminates these weakly antigenic species.

Dwg.0/5

FS CPI

FA AB: D

MC CPI: B04-B04C2; B04-F02A; B04-F10; B04-F11; B04-G01; B04-N03; B05-A01B; B05-B02C; B05-C08; B07-A02B; B14-A01; B14-A02; B14-H01; B14-L01;

B14-L06; **B14-S11**; **D05-H07**; D05-H08; D05-H11

TECH

UPTX: 20021014

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The growing step involves exposing the cells containing the tumor antigen, bacterial protein or viral protein to adenosine dialdehyde under 15 - 30 microM adenosine dialdehyde at approximately 25 - 40 degrees Centigrade for 1 - 5 days. The treating step involves exposing the tumor antigen, bacterial protein or viral protein or its fragment to acidic methanol or carbon dioxide (1 - 20%).

Preferred Cells: The tumor cells are selected from murine B16 melanoma, P815 murine mastocytoma, PTAS murine mammary carcinoma, colon rectal carcinoma, adenocarcinoma, glioblastoma multiform and astrosarcoma, cervical carcinoma, lung carcinoma, lymphomas, fibrosarcoma or myeloma. The tumor antigen is MART-1 (Melan-A), gp100 (pmel-17), tyrosinase, tyrosinase related protein-1 (TRP-1), tyrosinase related protein-2 (TRP-2), melanocyte-stimulating hormone receptor, beta-catenin, MUM-1, CDK-4, Caspase-8, KIA0205, MAGE-1, MAGE-2, MAGE-3, MAGE-12, BAGE, GAGE, Ny-ESO-1, alpha-Fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic antigen (CEA), p53 or Her-2/neu. The bacterial cells are selected from Bacillus, Mycobacterium, Streptococcus, Staphylococcus, Neisseria, Chlamydia, Haemophilus, and Borrelia burgdorferi. The viruses are Hepatitus A, Hepatitus B, Hepatitus C, Rabies, HIV, influenza, Measles, Rotavirus or Herpes simplex.

Preferred Proteins: The bacterial protein is PhoE, OmpF, OmpC, LamB, O-antigens, lipoproteins, flagella proteins or bacterial adhesions. The viral protein is HIV gp120, gp41, Hepatitis B surface antigens (HBsAg), core antigen (HbcAg) or capsid proteins.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (a) or (b) comprises an amino acid sequence selected from Asn-Gly, Asn-Ser, Asp-Gly or Asp-Ser. The peptide comprises 9 - 25 (preferably 9 - 15) amino acid residues. The peptide has a sequence Tyr-Met-Asp-Gly-Thr-Met-Ser-Gln-Val. Preferred Carrier: The carrier is solid carrier material, electrolyte solutions, anal suppositories, topical creams, sublingual lozenges, water

soluble jellies, enema solutions, inhalable aerosols and/or intravenous injections or is magnesium carbonate, magnesium stearate, talc, sugar, lactose, cocoa butter, and/or water.

TECHNOLOGY FOCUS - POLYMERS - Preferred Carrier: The carrier is pectin, dextrin, starch gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, and/or low melting waxes.

ABEX

UPTX: 20021014

ADMINISTRATION - The **vaccine** or composition containing (I) is administered intravenously, intramuscularly, intracutaneously, subcutaneously, subdermally, intraperitoneally, by inhalation, or intranasally. The dosages of (I) are 0.5 - 15 mg/kg.

EXAMPLE - Mice were immunized with either isoaspartyl modified tumor cell lysate or unmodified tumor cell lysate. After 14 days, purified CD8 T cells were purified from mice and incubated for 7 days with irradiated B16 tumor cells and interleukin-2. After 7 days, T cells were re-purified and incubated with labeled B16 melanoma cell targets at 20:1 (effector T cell:tumor cell ratio). Percent lyris was measured by the release of intracellular label as compared to control B16 cell cultures. The results showed that the CD8 T cell from isoaspartyl immunized mice had approximately 20 - 25% of tumor cell killing activity, while the control untreated animals had less than 5% killing activity of the target B16 cells.

L118 ANSWER 4 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 2002-454534 [48] WPIX

DNC C2002-129220

TI Use of adhesion protein from yersinia genus or its fragment in new adjuvant composition useful as medicament in treatment of e.g. allergy.

DC B04 D16

IN HERMAND, P; VANDE VELDE, V

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS

CYC 95

PI WO 2002030458 A1 20020418 (200248)* EN 46p A61K039-39 <-RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001062163 A 20020422 (200254) A61K039-39

ADT WO 2002030458 A1 WO 2001-EP3786 20010326; AU 2001062163 A AU 2001-62163 20010326

FDT AU 2001062163 A Based on WO 200230458

PRAI GB 2000-25058 20001012

IC ICM A61K039-39

ICS A61P031-00; A61P033-00; A61P035-00

AB WO 200230458 A UPAB: 20020730

NOVELTY - An adjuvant composition (I) comprises an adhesion protein from Yersinia genus or its fragment.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine composition comprising the adjuvant

further comprising an antigen or antigen composition; and

(2) use of Yersinia adhesion protein in the manufacture of (I). ACTIVITY - Antibacterial; Virucide; Antiallergic; Cytostatic;

Immunosuppressive; Antiarteriosclerotic; Nootropic; and Neuroprotective.

MECHANISM OF ACTION - None given.

USE - As medicament in the treatment of or in the manufacture of a mucosal **vaccinal** for the treatment of viral, bacterial, parasitic infections, allergy, cancer (claimed) such as prostate, breast,

colorectal, lung, pancreatic, renal, ovarian and melanoma, autoimmune disease, other non-chronic disorders, chronic disorders such as atherosclerosis and Alzheimer.

ADVANTAGE - The **adjuvant** induces or boosts immune responses to co-administered antigens. The **adjuvant** systems are safe and potent and are easy to manufacture. The **adjuvant** system exhibits good safety profile and is well tolerated by patients. Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-F10A; B04-F10B; B04-F11; B14-A01; B14-A02; B14-B02; B14-G03; B14-H01; B14-J01A4; **B14-S11**; **D05-H07**; D05-H17A6

UPTX: 20020730

TECH

TECHNOLOGY FOCUS - BIOLOGY - Preferred Composition: The composition optionally comprises a carrier. The composition additionally comprises another immunostimulant. The **adjuvant**:antigen is in a ratio of 1:1000 - 1000:1. The composition further comprises an excipient or diluent.

Preferred Components: The adhesion protein is encoded by the inv gene of Yersinia pseudotuberculosis, the inv gene of Yersinia enterocolitica or by ail gene of Yersinia enterocolitica. The immunostimulant is 3D-MPL, QS21, CpG, polyoxyethylene ether or ester. The antigen is optionally linked to the adjuvant through a direct or indirect linkage. The antigen is human immunodeficiency virus, varicella zoster virus, herpes simplex virus type 1, herpes simplex virus type 2, human cytomegalovirus, dengue virus, hepatitis A, B, C or E, respiratory syncytial virus, human papilloma virus, influenza virus, hib, meningitis virus, salmonella, neisseria, borrelia, chlamydia, bordetella, enterotoxic E. coli, campylobacter, streptococcus, moraxella, mycoplasma, mycobacteria, haemophilius, plasmodium or toxoplasma, standworth decapeptide or tumor associated antigen (TAA), MAGE, BAGE, GAGE, MUC-1, Her-2 neu, LnRH, CEA, PSA, PSMA, PAP, prostase, KSA, tyrosinase or PRAME or is Lipo-OspA from Borrelia burgdorferi, campylobacter whole cells or tetanus toxoid.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The carrier is metallic salt particle such as aluminum phosphate, aluminum hydroxyde, calcium phosphate, magnesium phosphate, iron phosphate, calcium carbonate, magnesium carbonate, calcium sulfate, magnesium hydroxyde or double salts such as ammonium-iron phosphate, potassium-iron phosphate, calcium-iron phosphate, calcium-magnesium carbonate or a porous polymeric particle such as microbead or nanoparticle.

ABEX

UPTX: 20020730

WIDER DISCLOSURE - The expression vectors are also disclosed as new.

ADMINISTRATION - The adjuvant system is administered mucosally, systemically or parenterally (including intramuscularly, intradermally, transdermally, subcutaneously, intraperitoneally or intravenously), orally, nasally vaginally or rectally in a dosage of 1-1000 (preferably 1-500, especially 1-100) microg/dose.

EXAMPLE - No relevant example given.

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L118 ANSWER 5 OF 14 WPIX (C) 2003 THOMSON DERWENT
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AN 2002-382792 [41] WPIX

DNC C2002-107821

TI Sustained release composition for treating e.g. multiple sclerosis, comprises microparticles containing an active agent, a biocompatible polymer and a water-soluble polymer.

DC A96 B04 D16

IN SCHER, D S; TRACY, M A

PA (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS

CYC 97

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PI WO 2002015877 A2 20020228 (200241)* EN 38p A61K009-00 <-RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001085143 A 20020304 (200247) A61K009-00

ADT WO 2002015877 A2 WO 2001-US26094 20010821; AU 2001085143 A AU 2001-85143 20010821

FDT AU 2001085143 A Based on WO 200215877

PRAI US 2000-644631 20000823

IC ICM A61K009-00

AB WO 200215877 A UPAB: 20020701

NOVELTY - A sustained release composition comprising microparticles containing an antigen or a labile agent, a biocompatible polymer and a water soluble polymer representing 20 % of the dry weight of microparticles, is new.

DETAILED DESCRIPTION - A new sustained release composition comprises microparticles containing an antigen or a labile agent, a biocompatible polymer and a water soluble polymer representing 20 % of the dry weight of microparticles, where the microparticles have a number median diameter of greater than 20 microns upon administration and generate pseudo-microparticles upon hydration having a number median diameter of less than 20 microns.

ACTIVITY - Immunosuppressive; Dermatological; Antiinflammatory; Neuroprotective; Antiviral; Antibacterial; Antiprotozoal; Antifungal; Antiallergic. No suitable biological data is given.

MECHANISM OF ACTION - Systemic immune response stimulator; Immune response modulator; Vaccine.

USE - The composition is used:

- (i) for stimulating a systemic immune response to an antigen representing cell (e.g. dendritic cell or macrophage Kupffer cell, aveolar macrophage, microglial cell, splenic macrophage and/or macrophage in the Peyer's of the gut) in a mammal;
- (ii) for the systemic delivery of a labile agent to a mammal; and (iii) for modulating an immune response of the composition (all claimed).

It is also used for the targeted delivery of biological active agents to specific tissue and cells and for treating autoimmune disease e.g. systemic lupus erythematosus and multiple sclerosis and treatment of conditions exacerbated by the activity of macrophages e.g. schistosomiasis.

ADVANTAGE - The composition provides the dissolution of the water-soluble polymer at a much greater rate than the degenerative of the biocompatible polymer. This variance in solubility generates pseudo-microparticles having a number mean diameter of at most about 20 (preferably at most 10 especially 1 - 5) microns which is substantially smaller than the size of the administered microparticles (number median diameter of at least 20 microns). The generation of pseudo-microparticles overcomes the problems associated with the processing and handling of small microparticles. A small delivery device is needed to obtain delivery of sufficient levels of the agent. A single dose of the composition is sufficient to result in long term and even permanent immunity to the incorporated antigen.

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-B03C; B04-B04C; B04-C03; B04-H01; B04-H02; B04-H04B; B04-H04C; B04-H05; B04-H06; B04-H06F; B04-H08; B04-H09; B04-H13; B04-N04; B05-A01A; B05-A01B; B05-A03A; B07-A02A; B10-D01; B14-A01; B14-A02; B14-A03; B14-A04; B14-B03; B14-C03; B14-G01; B14-G02A; B14-J01; B14-J02; B14-N17C; B14-S01; B14-S11;

D05-H07; D05-H10; D05-H18 UPTX: 20020701

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The composition is enterically coated and further comprises a cytokine and a metal cation component dispersed within the biocompatible polymer. TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The cytokine is selected from interleukin (IL)-1(alpha or beta), IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, granulocyte macrophage-colony stimulating factor (GM-CSF), M-CSF, leukemia inhibitory factor (LIF); leukotriene (LT), transforming growth factor (TGF)-beta, gamma-IFN (interferon), alpha-IFN, -beta-IFN, tumor necrosis factor (TNF)alpha, B Cell Growth Factors (BCGF), CD2 ICAM (intercellular adhesion molecule) MAdCAM or monocyte chemotactic protein (MCP)-1-3. The cytokine and antigen are co-incorporated into the microparticles or incorporated into separate microparticles. The separate microparticles are administered simultaneously or sequentially. The antigen is an allergen, viral antigen, bacterial antigen, protozoan antigen or a fungal antigen, (preferably influenza antigen, respiratory syncytial antigen, parainfluenza virus, helminthic pathogen antigen, Staphylococcus antigen, Hemophilius antigen or an antigen to vaccinate against allergies, especially a DNA-based vaccine, comprising plasmid DNA. The antigen is present at a concentration (w/w.%) of 0.01 - 50 (preferably 0.01 - 30). The labile agent is a protein, polypeptide or oligonucleotide (preferably

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer: The water-soluble polymer is a nonionic surfactant (preferably poloxamers, polysorbates, polyethyleneglycols and/or polyvinylpyrrolidones especially poloxamer 188 and/or poloxamer 407 or polysorbate 80 and/or polysorbate 20). The water-soluble polymer (%) is present in an amount at least 40 (preferably 40 - 60, especially 40 - 50). The biocompatible polymer is biodegradable and is selected from poly(lactide)s, poly(glycolide)s, poly(lactide-coglycolide)s, poly(lactic acid)s, poly(glycolic acid)s, poly(lactic acid-co-glycolic acid)s, poly(caprolactone), polycarbonates, polyestermide, polyanhydrides, poly(amino acid)s, poly(ortho esters)s, polycyanoacrylates, polyamides, polyacetals, poly(ether ester)s, copolymers of poly(ethylene glycol) and poly(ortho ester)s, poly(dioxanone)s, poly(alkylene alkylate)s, biodegradable polyurethanes, blends and/or copolymers (preferably poly(lactide-co-glycolide).

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The labile agent is complexed to a stabilizing metal cation. The metal cation is selected from Zn+2, Ca+2, Cu+2, Mg+2 and/or K+. The metal cation component is dispersed within the biocompatible polymer and is selected form Mg(OH)2, MgCO3, CaCO3, ZnCO3, Mg(OAc)2, Zn(OAc)2, ZnSO4, MgCl2, ZnCl2, MgSO4, zinc citrate or magnesium.

citrate.

Preparation: The composition is produced by standard chemical techniques.

UPTX: 20020701

SPECIFIC COMPOUNDS - Bordetella pertussis, Neisseria gonorrhea, Streptococcus pneumoniae and Plasmodium falciprum are specifically claimed as the antigen.

ADMINISTRATION - The composition is administered orally or parenterally (claimed) e.g. by inhalation or injection, implantation (e.g. subcutaneously, intramuscularly, intraperitoneally, intracranially or intradermally), intravaginally, intrapulmonary, bucally or by a suppository or by in situ delivery e.g. enema or aerosol spray.

EXAMPLE - Trehalose containing microparticles were prepared using a poly(lactide-Co-glycolide) (PLG) (10 w/v%) solution in methylene chloride in the polymer solution. A portion of microparticles were incubated for 2 hours at 37 degrees Centigrade in pH 7.2 phosphate buffered saline (sodium

TECH

ABEX

a protein).

phosphate (50 mM), NaCl (100 mM), sodium azide (0.02 %)). The buffer was removed and the microparticles were dried by lyophilization. The pre-hydration and post-hydration particle size (micrometers) of the microparticles were 47.6 and 1.4 respectively.

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L118 ANSWER 6 OF 14 WPIX
                            (C) 2003 THOMSON DERWENT
     2002-257549 [30]
                       WPIX
ΑN
    C2002-076670
DNC
ТT
     New solid dose vaccine formulation in the form of a quick
     dissolving cake useful for oral administration in the treatment of
    melanoma comprises an antigen and an excipient.
DC
     B04 D16
    VANDE-VELDE, V
ΙN
     (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
PA
CYC
    WO 2002013858 A1 20020221 (200230)* EN
PΙ
                                              32p
                                                     A61K039-39
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
            SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
                                                     A61K039-39
     AU 2001086168 A 20020225 (200245)
    WO 2002013858 A1 WO 2001-IB1711 20010814; AU 2001086168 A AU 2001-86168
ADT
     20010814
    AU 2001086168 A Based on WO 200213858
FDT
PRAI GB 2000-20089
                      20000815
TC
     ICM A61K039-39
         A61K009-20; A61K039-00; A61K039-02;
     ICS
          A61K039-12
    WO 200213858 A UPAB: 20020621
AB
    NOVELTY - An oral solid dose vaccine composition comprises an
     antigen and an excipient. The vaccine is in the form of a quick
     dissolving cake.
          ACTIVITY - Cytostatic; Antiallergic; Antitumor; Immunostimulant. No
     biodata is provided in the source material.
          MECHANISM OF ACTION - Vaccine.
          USE - For oral administration in the treatment of immunotherapeutic
     treatment of cancer, melanoma; for the prophylaxis or therapy of allergy.
     For treatment of tumor. For eliciting and stimulating an immune response
     against a human pathogen.
          ADVANTAGE - The formulation after insertion into mouth, rapidly
     dissolves in saline, thus releasing the vaccine into the mouth.
     Dwq.0/0
    CPI
FS
    AB; DCN
FΑ
MC
     CPI: B04-B04C2; B04-C02; B04-C02C; B04-C02D; B04-C03; B05-A01B; B05-C04;
          B07-A02A; B07-A02B; B10-A07; B12-M11; B12-M11B; B14-A02A; B14-A02B;
          B14-G01; B14-G02A; B14-H01; B14-S11; B14-S11C;
          D05-H07
TECH
                    UPTX: 20020513
     TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The composition
     comprises an antacid, dextran, binding agent, pseudoplastic excipient,
     thixotropic agent, live attenuated or viral vaccine or
     stabilizing glass forming polyol. The composition additionally comprises
     sorbitol and adjuvant selected from LT, CT, 3D-MPL, CpG, or
     OS21.
     Preferred Method: The cake is formed by sublimation of a liquid
     vaccine composition.
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TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Antacid: The antacid is aluminum hydroxide and/or magnesium hydroxide or calcium carbonate.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The polyol is trehalose, sucrose, lactose, fructose, galactose, mannose, maltulose, iso-maltulose, lactulose, maltose, dextrose or their respective sugar alcohol (preferably mannitol, lactitol or maltitol).

TECHNOLOGY FOCUS - BIOLOGY - Preferred Antigen: The antigen or antigen composition is derived from Human Immunodeficiency Virus, Varicella Zoster virus, Herpes Simplex Virus type 1, Herpes Simplex Virus type 2, human cytomegalovirus, Dengue virus, Hepatitis A, B, C or E, Respiratory Syncytial virus, Human papilloma virus, Influenza virus, Hib, Meningitis virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Plasmodium or Toxoplasma, stanworth decapeptide or tumor associated antigens (TMA), MAGE, BAGE, GAGE, MUC-1, Her-2 neu, LnRH, CEA, PSA, KSA or PRAME.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The pseudoplastic excipient is xanthan gum. The binding agent is dextran. The composition comprises xanthan gum, dextran and calcium hydroxide or aluminum hydroxide.

ABEX

UPTX: 20020513

ADMINISTRATION - The **vaccine** composition is administered orally (claimed) in a dosage of 1 - 1000 (preferably 1 - 500, especially 1 - 100; particularly 1 - 50) microg of protein.

EXAMPLE - Frozen purified viral bulk was thawed and diluted with Dulbecco's modified eagle medium (106.2 ffu/ml). Aluminum hydroxide was

Dulbecco's modified eagle medium (106.2 ffu/ml). Aluminum hydroxide was added to reach a final quantity of 48 mg/dose and virus composition was diluted with sucrose (4%) up to the target titer of 105.6 ffu/dose. An aseptic filling operation was employed to transfer doses of plastic blister cavities (0.5 ml). Thus the formulation contained sucrose (4%), sodium glutamate (3.7%) and aluminum hydroxide (3.48 mg). The composition was lyophilized and the blister cavities were sealed by thermic sealing. The formulation was tested for virus titer before and after lyophilization into a cake and stored before and after titer lyophilization of 1 week at 37 degrees C. The viral titer before and after lyophilization for 1 week at 37 degrees C was 105.11 and 104.53 respectively. These formulation rapidly dissolved in the mouth.

L118 ANSWER 7 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 2002-188810 [24] WPIX

DNC C2002-058450

TI Adjuvant useful in parenteral vaccine

formulation which generates immune response, comprises salt(s) formed with e.g. magnesium, calcium, strontium, barium, radium, titanium, zirconium, hafnium, or rutherfordium.

DC B04 B06

IN AASMUL-OLSEN, S; LUND, L; RAHBEK, J U; SONI, N K

PA (ALKA-N) ALK-ABELLO AS

CYC 96

PI WO 2002011760 A1 20020214 (200224)* EN 53p A61K039-39 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2002051794 A1 20020502 (200234) A61K039-00 <-AU 2001079601 A 20020218 (200244) A61K039-39 <--

ADT WO 2002011760 A1 WO 2001-DK532 20010809; US 2002051794 A1 Provisional US 2000-224037P 20000809, US 2001-925635 20010809; AU 2001079601 A AU 2001-79601 20010809

FDT AU 2001079601 A Based on WO 200211760

PRAI US 2000-224037P 20000809; **DK 2000-1194 20000809**

IC ICM A61K039-00; A61K039-39

ICS A61K039-38; A61K045-00; A61K047-00; A61P037-04

AB WO 200211760 A UPAB: 20020416

NOVELTY - An adjuvant (A) comprises salt(s) formed with magnesium, calcium, strontium, barium, radium, titanium, zirconium, hafnium, or rutherfordium or their hydrates, provided that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminum hydroxide or aluminum oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

 ${\tt DETAILED}$ <code>DESCRIPTION</code> - <code>INDEPENDENT</code> <code>CLAIMS</code> are included for the following:

- (1) a parenteral vaccine formulation comprising at least one immunogenic substance and (A);
 - (2) (A) for parenteral use;
- (3) use of salt(s) formed with magnesium, calcium, strontium, barium, radium, titanium, zirconium, hafnium, or rutherfordium or their hydrates, as a component of an adjuvant composition, provided that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminum hydroxide or aluminum oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine;
- (4) generating immune response in a subject comprising administering the parenteral vaccine formulation; and
- (5) preparation of parenteral vaccine formulation comprising adding liquid to a dry foam of or a pre-formed gel of the salt formed with magnesium, calcium, strontium, barium, radium, titanium, zirconium, hafnium, or rutherfordium or their hydrates, (provided that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminum hydroxide or aluminum oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine) to obtain an adjuvant composition; and mixing the adjuvant composition with immunogenic substance(s) and optionally with carriers and/or excipients to obtain the parenteral vaccine formulation.

ACTIVITY - Immunostimulant.

MECHANISM OF ACTION - Vaccine.

No details of tests showing mechanism of action are given.

USE - The adjuvant is useful in the parenteral

vaccine formulation which is useful for generating an immune
response in a subject (a vertebrate, e.g. human) following administration
of the vaccine formulation, (claimed).

ADVANTAGE - The adjuvant may create a depot of antigen resulting in a prolonged slow release over time, therefore reducing the need for booster vaccinations.

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: B04-A07E; B04-B04C; B05-A01B; B05-A03B; B05-B02A3; B05-B02C; B05-C04; B05-C05; B05-C08; **B14-S11**

TECH UPTX: 20020416

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Salt(s): The salt is an inorganic or organic salt, formed with oxides, peroxides, hydroxides, carbonates, phosphates, pyro-phosphates, hydrogenphosphates, dihydrogenphosphates, sulfates and/or silicates and their hydrates, (preferably salts formed between magnesium, calcium, barium, titanium or zirconium and oxide, peroxide, hydroxide and/or carbonate, and their hydrates).

Preferred Adjuvant: The formulation further comprises an additional adjuvant selected from saponins (sterol and triterpenoid glycosides, derived from bark of Quilaja saponiaria tree) such as Quil A, Qa-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminum salts. The formulation further comprises carriers and/or

excipients such as diluents, buffers, suspending agents, solubilizing agents, pH-adjusting agents, dispersing agents and/or colorants. The cation of the adjuvant is present in amount of 0.0004-120 (preferably 0.008-6) M.

ABEX

UPTX: 20020416

SPECIFIC COMPOUNDS - The use of 34 compounds as the salt are claimed, e.g. magnesium hydroxide, magnesium

carbonate hydroxide pentahydrate, beryllium oxide (sic), titanium dioxide, calcium carbonate, barium hydroxide,

barium peroxide, barium carbonate, barium sulfate, calcium sulfate, tricalcium silicate, calcium pyrophosphate, calcium dihyrogenphosphate, calcium sulfate dihydrate, magnesium carbonate,

magnesium sulfate, trimagnesium phosphate, magnesium silicate, titanium disulfate, zirconium sulfate and strontium carbonate (preferably

magnesium hydroxide, magnesium

carbonate hydroxide pentahydrate and/or titanium
dioxide).

ADMINISTRATION - The parenteral vaccine can be administered, e.g. by intravenous, intramuscular, intraarticular, subcutaneous, intradermal, epicutantous and intraperitoneal routes.

EXAMPLE - No relevant example is given.

L118 ANSWER 8 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 2000-532864 [48] WPIX

DNC C2000-158763

TI Composition for the delivery of a biologically interactive substance, e.g. a medicament, via a mucosal membrane of a vertebrate comprises a mucosal delivery system with an oxygen-containing metal salt.

DC B04 B07 D16

IN IPSEN, H H; ULDAL RAHBEK, J

PA (ALKA-N) ALK-ABELLO AS

CYC 91

PI WO 2000045847 A1 20000810 (200048)* EN 95p A61K047-02 <-RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000022797 A 20000825 (200059)

A61K047-02 <--

EP 1146906 A1 20011024 (200171) EN A61K047-02 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CN 1338947 A 20020306 (200236) A61K047-02 <--

ADT WO 2000045847 A1 WO 2000-DK49 20000204; AU 2000022797 A AU 2000-22797 20000204; EP 1146906 A1 EP 2000-901497 20000204, WO 2000-DK49 20000204; CN 1338947 A CN 2000-803452 20000204

FDT AU 2000022797 A Based on WO 200045847; EP 1146906 Al Based on WO 200045847 PRAI US 1999-118896P 19990205; DK 1999-115 19990205

IC ICM A61K047-02

AB WO 200045847 A UPAB: 20001001

NOVELTY - A composition for the delivery of a biologically interactive substance via a mucosal membrane of a vertebrate comprising a biologically interactive substance and a mucosal delivery system (A) with an oxygen-containing metal salt, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a **vaccine** for the delivery of an immunogenic substance via a mucosal membrane of a vertebrate comprising an immunogenic substance and (A);
 - (2) a formulation for the delivery of a nutritional substance via a

mucosal membrane of a vertebrate comprising a nutritional substance and (A);

- (3) a formulation for the delivery of a medicament via a mucosal membrane of a vertebrate comprising a medicament and (A);
- (4) a formulation for the delivery of genetic material via a mucosal membrane of a vertebrate comprising genetic material and (A);
- (5) a mucosal delivery system for delivery of a biologically interactive substance via a mucosal membrane of a vertebrate comprising an oxygen-containing metal salt;
- (6) delivery of a biologically interactive substance via a mucosal membrane of a vertebrate, including a human, comprising administering the new composition;
- (7) generating an immune response in a vertebrate, including a human, comprising administering (1) to the vertebrate;
- (8) **vaccination** or treatment of a vertebrate, including a human comprising administering the new composition or one of (1) (4);
- (9) treating, preventing or alleviating allergic reactions or infectious diseases comprising administering (1) to a vertebrate, including a human;
 - (10) preparing (5) using an oxygen-containing metal salt;
 - (11) using antibodies raised by administering (1);
- (12) preparing the new composition or one of (1) (4) by mixing (5) with a biologically interactive substance, and optionally pharmaceutically acceptable excipients; and
- (13) a composition, **vaccine** or formulation obtainable by (12).

ACTIVITY - Antiallergic; antiinflammatory; immunostimulant. No biological data is given.

MECHANISM OF ACTION - Vaccine. No biological data is given.

USE - An oxygen-containing metal salt is used to prepare (A) which delivers a biologically interactive substance, such as an immunogenic substance, a nutritional substance, a medicament or genetic material, to a vertebrate via a mucosal membrane. A composition, vaccine or formulation comprising (A) and the biologically interactive substance is used for administration to allow delivery of the substance. The vaccine is used for the treatment, prevention or alleviation of allergic conditions or infectious diseases. The vaccine generates an immune response and vaccinates a vertebrate (all claimed).

ADVANTAGE - The biologically interactive substance is administered via a mucosal membrane of a vertebrate and avoids conventional parenteral vaccination which has to be performed by a physician and is often inconvenient for the patient. Parenteral administration can also be unpleasant.

Dwg.0/27

FS CPI

FA AB; DCN

MC CPI: B03-L; B04-A04; B04-B04C2; B04-B04C7; B04-C01A; B04-D01; B04-E01; B04-F10; B04-F11; B04-G01; B04-H02; B04-J01; B04-L01; B04-L04; B04-M01; B04-N04; B04-N0400E; B11-C04; B12-M11F; B14-A01; B14-C03; B14-G01; B14-G02A; B14-S11; D05-H07

TECH UPTX: 20001001

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The biologically interactive substance is an immunogenic substance, a nutritional substance, a medicament, genetic material, or analogs or derivatives of them. The immunogenic substances are natural, recombinant or modified proteins, fragments of them, antigens, allergens, allergoids, peptides, haptens, carbohydrates, optionally inactivated or attenuated bacteria or virus as well as components of them, RNA, DNA, PNA, parasites or retroviruses, parasitic material, mycoplasma, toxins, or analogs or derivatives of them. The nutritional substance is a vitamin, salt, enzyme, trace element, trace mineral, or an analog or derivative of them.

The medicament is an antibody, antibiotic, peptide, salt, hormone, hemolytic, haemostatic, enzyme inhibitor, or an analog or derivative of them. The genetic material is RNA, DNA, PNA, or an analog or derivative The enzyme is urokinase, tissue plasminogen activator, of them. coagulation factor VIII, streptokinase, or an analog or derivative of them. The cation of the oxygen-containing metal salt is Al, K, Ca, Mg, Zn, Ba, Na, Li, B, Be, Fe, Si, Co, Cu, Ni, Ag, Au, or Cr. The anion of the oxygen-containing metal salt is a sulfate, hydroxide, phosphate, nitrate, iodate, bromate, carbonate, hydrate, acetate, citrate, oxalate, tartrate, or a mixed form of these. The oxygen-containing metal salt is aluminium hydroxide, aluminium phosphate, aluminium sulfate, aluminium acetate, potassium aluminium sulfate, calcium phosphate, calcium tartrate, maalox (mixture of aluminium hydroxide and magnesium hydroxide), beryllium hydroxide, zinc hydroxide, zinc carbonate, barium sulfate or zinc sulfate. The composition further comprises a bioadhesive. It further comprises a pharmaceutically acceptable adjuvant such as interleukins (e.g. IL-1 beta, IL-2, IL-7, IL-12, and INF gamma), Adju-Phos (RTM), glucan, antigen formulation, Cholera Holotoxin, liposomes, DDE, dehydroepiandrosterone, DMPC, DMPG, DOC/Alum Complex Freund's incomplete adjuvant, ISCOMs (RTM), LT Oral Adjuvant, muramyl dipeptide, monophosphoryl lipid A, muramyl tripeptide, and phospatidylethanolamine. The mucosal membrane is nasal, buccal, sublingual or gastrointestinal. Preferred Formulation: The medicament is a beta-lactam, a sulfa-containing preparation, an enzyme inhibitor, a hormone, a hemolytic/haemostatic, a psychoactive drug, an opiate, a barbiturate, an enzyme, or a cancer-related compound.

ABEX UPTX: 20001001

ADMINISTRATION - Dose is 0.1 - 100 (preferably 1 - 10) times as large as a parenteral bioequivalent dose. Administration is via oral (preferred), nasal, vaginal, sublingual, ocular, rectal, urinal, intramammal, pulmonal, otolar (via the ear), or buccal routes (claimed). The composition, vaccine, or formulation is administered in the form of a spray, an aerosol, a mixture, tablets (entero- or not-enterocoated), capsules (hard or soft, entero- or not-enterocoated), a suspension, a dispersion, granules, a powder, a solution, an emulsion, chewable tablets, tablets for dissolution, drops, a gel, a paste, a syrup, a cream, a lozenge (powder, granulate, tablets), an instillation fluid, a gas, a vapor, an ointment, a stick, implants (ear, eye, skin nose, rectal, or vaginal), intramammary preparations, vagitories, suppositories, or uteritories (claimed).

EXAMPLE - A composition comprising an immunogen and oxygen-containing metal salt was formed. The immunogen (allergen extract or Tetanus toxoid) was dissolved or diluted to a concentration 10 times the concentration of the final formulation. 1/10 vol immunogen solution was mixed with 7/10 vol Coca 0.0 buffer (0.25 percent sodium hydrogen carbonate and 0.5 percent sodium chloride). 2/10 vol Alhydrogel (RTM) 1.3 percent was slowly added. The preparations were stored for no more than 3 weeks. The formulations comprising oxygen-containing metal salts and T. toxoid were stored at 4 degrees Centigrade.

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L118 ANSWER 9 OF 14 WPIX (C) 2003 THOMSON DERWENT
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AN 2000-505101 [45] WPIX

DNN N2000-373464 DNC C2000-151561

TI New spatially aligned conjugated composition having a thioether bond linkage, useful as an immunogen or **vaccine** against virus, bacteria (e.g. rickettsiae or chlamydiae), protozoa, fungal or parasitic infectious agents.

DC B04 C03 D16 P34

IN FREY, A; NEUTRA, M R; ROBEY, F A

PA (CHIL-N) CHILDRENS MEDICAL CENT

CYC 1

PI US 6086881 A 20000711 (200045)* 27p A61K039-385 <-ADT US 6086881 A US 1998-79374 19980515.

PRAI US 1998-79374 19980515

IC ICM A61K039-385

ICS A61K038-00; A61M036-14; C07K005-00

AB US 6086881 A UPAB: 20000918

NOVELTY - A spatially aligned conjugated composition used to induce an immune response against an infectious agent, is new. The conjugated composition comprises at least one chemically modified substance, several chemically substituted metallic oxide particles, and at least one thioether bond joining the modified substance in a controlled orientation to the substituted metallic oxide particles.

DETAILED DESCRIPTION - A spatially aligned conjugated composition used to induce an immune response against an infectious agent, is new. The conjugated composition comprises at least one chemically modified substance, several chemically substituted metallic oxide particles, and at least one thioether bond joining the modified substance in a controlled orientation to the substituted metallic oxide particles.

The chemical modification provides the substance with at least one reactive entity and a fixed spatial orientation for forming a thioether bond. The substance is selected from haptens and antigens immunologically representative of the infectious agent. The chemical substitution provides the particles with at least one corresponding reactive moiety for forming a thioether bond. The metallic oxide particles have a diameter of 10-10000 nm.

An INDEPENDENT CLAIM is also included for a fluid immunogen to be administered to a subject for inducing an immune response against an infectious agent. The fluid immunogen comprises a biocompatible carrier fluid, and the spatially aligned conjugated composition.

ACTIVITY - Antibacterial; protozoacide; antifungal; antiparasitic. MECHANISM OF ACTION - Vaccine. The immunogenicity of the peptomer-particle conjugate (the conjugate composition) was tested in BALB/c mice. AntiHIVMN gp120 C4 domain peptomer serum response was tested. After priming and 3 booster immunizations, the humoral immune response was about 20-fold higher. Superior immunogenicity of the peptomer-particle antigen was also observed when analyzing the cross reactivity of the final anti-C4 domain IgG responses to native gp 120. Five out of six animals immunized with peptomer-particles, and 3 out of 4 animals immunized with peptomer-particles+MDP recognized baculovirus-expressed HIVMN gp120 in the final bleed.

USE - The composition is useful as an immunogen and as a vaccine. The composition induces an immune response against a virus, or a bacterium. The composition especially induces an immune response against rickettsiae, chlamydiae, mycoplasms, protozoa, fungal or parasitic infectious agents (all claimed). It is also useful as a diagnostic tool in any assay involving antibodies specific for the antigen or hapten indicative of an infectious agent. The composition may be employed for its spatial orientation and structural configuration properties in order to play any role in determining or evaluating the biological activity of novel peptides, proteins, or other pharmacological agents that are ostensibly biologically active.

Dwg.0/9

FS CPI GMPI

FA AB; DCN

MC CPI: B04-C02; B04-N03; B04-N04; B05-A01B; B05-A03B; B05-B02A3; B05-B02C;

B14-S11A; B14-S11B; C04-C02; C04-N03; C04-N04;

C05-A01B; C05-A03B; C05-B02A3; C05-B02C; C14-S11A;

C14-S11B; D05-H07; D05-H09

TECH UPTX: 20000918

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The chemically modified substance comprises a polysaccharide or a proteinaceous composition.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Composition: The

metallic oxide particles are composed of aluminum oxide, titanium dioxide, zirconium dioxide, hydroxyapatite, silicon dioxide, magnesium oxide, yttrium oxide, scandium oxide, or lanthanum oxide. The metallic oxides have a diameter of 40-900, preferably 300 nm.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Immunogen: The fluid immunogen comprises a biocompatible fluid carrier selected from physiological saline, an aqueous solution containing electrolytes, or a buffered aqueous liquid. The biocompatible fluid carrier is an oil-based formulation selected from petroleum, mineral or oil, or a water-in-oil emulsion. The fluid immunogen induces an immune response against a virus, or a bacterium. The fluid immunogen also induces an immune response against rickettsiae, chlamydiae, mycoplasms, protozoa, and fungal or parasitic infectious agents.

Preparation: The composition may be chemically synthesized under controlled chemical conditions.

ABEX

UPTX: 20000918

ADMINISTRATION - Administration may be systemic (e.g. parenteral, intravenous, intramuscular or intraperitoneal), or by localized routes, e.g. mucosal administration via the intragastric, nasal, rectal, oral or vaginal routes. No dosage given.

EXAMPLE - The peptomer of the human immunodeficiency virus (HIV) spatially aligned conjugated composition was a homopolymer of 18-mer oligopeptides $\verb|comprised| by the amino acid sequence: LysIleLysGlnIleIleAsnMetTrpGlnGluVal| \\$ GlyLysAlaMetTyrAlaCys. The HIVMN gp120 domain peptomer aluminum oxide nanoparticles were prepared by separately synthesizing the peptomer antigen and the metallic oxide particles, and conjugating both compounds in a terminal step. Initially, the peptide monomer for the preparation of the peptomer was synthesized as C-terminal amide on an automated peptide synthesizer. To allow subsequent head-to-tail polymerization via the intended thioether linkages, an additional cysteine was placed at the carboxy terminal end of the peptide chain. At the amino terminus, a bromoacetyl moiety was introduced. Typical yields of crude N-alpha-bromoacetyl-derivatized cysteine-containing peptide were between 50-70 %. After preparative high performance liquid chromatography (HPLC), 30 % of the expected pure peptide was obtained. Autopolymerization of the $\hbox{N-alpha-bromoacetyl-derivatized cysteine-containing peptide was initiated}$ by dissolving the purified peptide in aqueous buffer at slightly alkaline pH (pH 8.0). The peptomer was end-capped by completely removing the reactive groups at the head and tail of the polymer chain before it was prepared for side on conjugation by N-epsilon-bromoacetylation of the lysine side chains. Bromoacetylation of the lysines was carried out, and the randomly bromoacetylated peptomer was used for reaction with the thiol-modified particles. The thiol-modified, metallic oxide particles were prepared from plain alpha-aluminum oxide nanoparticles. To allow conjugation of the N-epsilon-bromoacetylated peptomer onto the particles via thioether linkages, the amine-modified alumina was reacted at pH 10 with a 100-fold molar excess of N-acetylhomosteinethiolactone. The formation of free thiol groups was assayed every 15 minutes with Ellmans' reagent. The thiol-derivatized aluminum oxide nanoparticles were then reacted with the N-epsilon-lysyl-bromoacetylated peptomer until no more free sulfyhydryl groups were detected in the reaction mixture. Amino acid analysis of the final conjugate revealed a 55 % coupling yield for the peptomer leading to a specific antigen load of 16 mg peptomer per g of aluminum oxide nanoparticles.

L118 ANSWER 10 OF 14 WPIX (C) 2003 THOMSON DERWENT

AN 1999-518367 [43] WPIX

DNC C1999-151281

TI Preparation of pharmaceutical compositions in the form of polymeric microparticles, useful for the preparation of tablets, capsules and packets..

```
A31 A32 A35 A96 B07
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                  T3 20020616 (200246)
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     19990205; KR 2001040727 A KR 2000-708611 20000805; IT 1298574 B IT
     1998-MI233 19980206; EP 1051158 B1 EP 1999-910199 19990205, WO 1999-EP781
     19990205; JP 2002502809 W WO 1999-EP781 19990205, JP 2000-530192 19990205;
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          A61K047-36; A61K047-44
AB
          9939692 A UPAB: 20011203
     NOVELTY - Pharmaceutical compositions are prepared in the form of
     polymeric microparticles.
          DETAILED DESCRIPTION - Preparation of pharmaceutical compositions in
     the form of polymeric microparticles comprises:
          (a) preparation of a homogeneous mixture of substances in powder form
     to which a liquid to pasty consistence is added;
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- (b) the extrusion of the mixture through a perforated mesh to obtain cylindrical filaments;
- (c) the spheronization of the filaments to obtain microparticles in spherical form;
 - (d) drying of the microparticles; and
 - (e) optional deposition of drug on the surface of the microparticles.

The mixture of substances in powder form comprises one or more cross-linked amphiphilic polymers and optionally one or more drugs, excipients, a bioadhesive substance and/or a substance having high density.

USE - The compositions are useful for the preparation of tablets, capsules and packets. The drugs may be drugs acting on the central nervous

system and on the peripheral nervous system, cardiovasculars, hypotensives, diuretics, anti-inflammatories, analgesics, antifebriles, antiasthmatics, bronchodilatators, antitussis, mucolytics, antibiotics, chemotherapeutic agents, antivirals, hormones, antineoplastics, immunosuppressants, immunostimulants, peptides, polypeptides, proteins and vaccines.

Dwg.0/1

FS CPI

FΑ AB; DCN

MC CPI: A11-A04; A11-B07B; A12-S09; A12-V01; B04-C01; B04-N02; B05-A01B; B10-C04D; B11-C09; B12-M11B; B12-M11C; B12-M11D; B14-A01; B14-A02; B14-C01; B14-C03; B14-C04; B14-D01; B14-F01; B14-F02; B14-F02B; B14-G01; B14-G02; B14-J01; B14-K01A; B14-K01B; B14-K01C; B14-K01D; B14-K01E; B14-N08; B14-S11 TECH

UPTX: 19991020

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred components: The cross-linked amphipilic polymers are selected from cross-linked polyvinyl pyrrolidone, sodium carboxymethyl cellulose, sodium glycolate starch and dextrans. The mixture in powder form consists of a cross-linked amphiphilic polymer and of a drug, obtained by high energy comilling or by loading by solvent. The bioadhesive substance is selected from alginates, scleroglucans, chitosans, xanthans and silicone gel. The high density substance is selected from aluminium oxide, titanium dioxide, iron oxide, calcium carbonate and barium sulfate. The liquid is selected from water, aqueous solutions, organic solvents and their mixtures, saturated and unsaturated natural oils, semisynthetic and synthetic mono-, di- and triglycerides, liquid waxes, silicone oils, polyethylene glycols, polyglycolic glycerides and polyglycols. Preferred drugs: The drugs are selected from drugs acting on the central nervous system and on the peripheral nervous system, cardiovasculars, hypotensives, diuretics, anti-inflammatories, analgesics, antifebriles, antiasthmatics, bronchodilatators, antitussis, mucolytics, antibiotics, chemotherapeutic agents, antivirals, hormones, antineoplastics, immunosuppressants, immunostimulants, peptides, polypeptides, proteins and vaccines.

Preferred process: The drugs are uniformly distributed inside the microparticles or deposited on the surface of the microparticles. When the drug is distributed inside the microparticles, it is present in an amount of 0.1-95% by weight with respect to the microparticles. Preferred composition: The amount of liquid is 1-80% by weight with respect to the mixture in powder form. The compositions comprise one or more cross-linked amphiphilic polymers, one or more drugs and optionally a bioadhesive substance and/or a high density substance, the microparticles having spherical or almost-spherical form with a diameter of 100 mum- 3

ABEX UPTX: 19991020

EXAMPLE - An extruder was fed with Explotab in the form of powder with granulometry lower than 140 mesh and with demineralized water and extrusion was carried out to give extrusion filaments. The filaments were treated in a spheronizator at a velocity of 800 rpm for 3 minutes to give a product in the form of microparticles which were dried in a stove at 70 degreesC for 12 hours.

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ΑN 1998-437043 [37] WPIX

1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36]; CR . 1998-031704 [03]; 1998-347245 [30]; 2001-396353 [42]; 2003-101718 [09]

DNC C1998-132804

TΙ New burst-free, sustained, programmable release composition(s) containing an active material in a blend of uncapped and end-capped co polymer, preferably a poly (DL-lactide-co glycolide).

A96 B04 B05 B07 D16 P73 DC

BOEDEKER, E C; FRIDEN, P; JACOB, E; JEYANTHI, R; MCQUEEN, C E; REID, R H; IN

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ROBERTS, F D; SETTERSTROM, J A; TICE, T R; VAN HAMONT, J E; BROWN, W;
     CASSELS, F; JARBOE, D L; THIES, C
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     ICM A61K009-50; A61K009-52
    ICS
        A61K047-30; B32B005-16
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    WO
          9832427 A UPAB: 20030206
    A composition is claimed for the burst-free, sustained, programmable
```

release of active material(s) over a period from 1-100 days, comprising: (a) an active material; and (b) a carrier which may contain pharmaceutically-acceptable adjuvant, comprised of a blend of uncapped and end-capped biodegradable-biocompatible copolymer.

Also claimed are: (1) a process for preparing controlled release compositions characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable poly(lactide/glycolide), in uncapped or end-capped form in methylene chloride, and dissolving a biologically active agent or active core in water; (b) adding the aqueous layer to the polymer solution and emulsifying to provide an inner water-in-oil (w/o) emulsion; (c) stabilising the w/o emulsion in a solvent-saturated aqueous phase containing a oil-in-water (o/w) emulsifier; (d) adding the w/o emulsion to an external aqueous layer containing o/w emulsifier to form a ternary emulsion; and (e) stirring the resulting water-in-oil-in-water (w/o/w) emulsion to remove the solvent, and rinsing hardened microcapsules with water and lyophilising the hardened microcapsules; (2) a method for the protection against infection of a mammal by pathogenic organisms comprising administering orally to the mammal an immunogenic amount of an immunostimulating composition consisting of an antigenic synthetic peptide encapsulated within a poly(lactide/galactide) matrix; (3) a vaccine for the immunisation of a mammal against infection by pathogenic organisms consisting of an antigen in an amount of 0.1-1%encapsulated within a biodegradable-biocompatible polymeric poly(DL-lactide-co-glycolide) matrix where the polymer is end-capped or a blend of uncapped and end-capped polymers; and (4) an immunostimulating composition comprising encapsulating-microspheres, which may contain an adjuvant, where the microspheres having a diameter of 1 nm to 10 microns are comprised of: (a) a biodegradable-biocompatible poly (DL-lactide-co-glycolide) as the bulk matrix, where the copolymer (lactide to glycolide L/G) ratio for uncapped and end-capped polymer is 0/100 to 1/99; and (b) an immunogenic substance comprising a bacteria, virus, fungus, parasite, or derivative, that serves to elicit the production of antibodies in animal subjects.

USE - The biocompatible and biodegradable microspheres can provide programmable sustained release of biologically active agents, including polypeptides over a period of up to 100 days in an aqueous physiological environment with little or no burst release. They can be used for the delivery of e.g. insulins, AZT, diethyl silbestrol, 17-beta-oestradiol, oestron, ethinyl estradiol, mestranol, norethindrone, norgestryl, ethynodiol diacetate, lynoestrenol, medroxyprogesterone acetate, dimethisterone, megestrol acetate, chlormadinine acetate, norgestimate, norethisterone, ethisterone, melentate, norgestimate, norethisterone, ethisterone, melentate, melengestrol, norethynodrel, nonylphenoxypolyoxyethylene glycol, benzethonium chloride, chlorindanol, aluminium hydroxide, calcium carbonate, magnesium carbonate, sodium carbonate, chloropromaquine HCl, clozapine, mesoridazine, metiapine, reserpine, thioridazine, chlordiazepoxide, diazepam, meprobamate, temazepam, codeine, phenobarbital, sodium pentobarbital, sodium secobarbital, testosterone, testosterone propionate, sulphonamides, 4-aminoquinolines, 8-aminoquinolines, pyrimethamine, mazindol. phentermine, L-dopa, atropine, methscopolamine bromide, dextromethorphan, noscapine, Rauwolfia alkaloids, nitroglycerin, organic nitrites, pentaerythriotetranitrate, potassium chloride, ergotamine with and without caffeine, hydrogenated ergot alkaloids, dihydroergocristine methanesulphate, dihydrooergocornine methanesulphonate, dihydroergokroyptine methanesulphate, atropine sulphate, Belladonna, hyoscine hydrobromide, dihydrocodienone, meperidine, morphine, salicylates, asprin, acetaminophen, d-propoxyphene, ceflacor, cefuroxime, chloramphenical, gentamycin, Kanamycin A, Kanamycin B, ampicillin, amoxicillin, streptomycin A, antimycin A, chloropamtheniol, metromidazole, oxytetracycline, penicillin G, minocycline, ciprofloxacin, ofoxacin, clarithromycin, frythromycin (sic), gentamicin, amikacin, tobramycin, kanamycin, ampicillin, polymyxin-B, amphotericin-B, aztrofonam, chloramphenicol, fusidans, lincosamides, metronidazole, nitro-furantion, imipenem/cilastin, quinolones, rifampin, polyenes, sulphonamides, trimethoprim, vancomycin, teicoplanin, imidazoles, mephenytoin, phenobarbital, trimethadione, triethylperazine, chlorophinazine, dimenhydrinate, diphenhydramine, perphenazine, tripelennamine, hydrocortisone, prednisolone, prednisone, allopurinol, indomethacin, phenylbutazone, prostaglandin, thiotepa, chloramucil, cyclophosphamide, melphalan, nitrogen mustard, methotrexate, aztreonam, and refampin. Dwg.0/54 CPI GMPI AB; DCN CPI: A05-E02; A10-E01; A12-V01; B02-P03; B04-B04C; B04-C03D; B04-F09; B04-F10; B04-F11; B12-M10A; B12-M11E; B14-G01; B14-S11; D05-H07 (C) 2003 THOMSON DERWENT L118 ANSWER 12 OF 14 WPIX 1993-182249 [22] WPIX 1992-024125 [03] DNC C1993-080684 Pasteurella multocida typed strain 4677 bacterin vaccine contain bordetella bronchiseptica and/or erysipelothrix rhusiopathiae bacterins used to inoculate animals against atropic rhinitis and erysipelas. B04 C06 D16 FRANTZ, J C; KEMMY, R J; ROBERTS, D S; SWEARINGIN, L A (PFIZ) PFIZER INC; (SMIK) SMITHKLINE BEECHAM CORP WO 9309809 A1 19930527 (199322)* EN 66p A61K039-00 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE W: AU CA JP US A 19930615 (199340) A61K039-00 <--AU 9331430 EN A61K039-00 <--EP 614371 A1 19940914 (199435) R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE

FS FΑ

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CR

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DC

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CYC PΙ

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     1992-US10008 19921113, US 1994-244052 19940711; JP 3270473 B2 WO
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    WO
          9309809 A UPAB: 20020418
       Vaccine compsn. comprises a Pasteurella multocida type D strain
```

Vaccine compsn. comprises a Pasteurella multocida type D strain 4677 bacterin with a cell-bound toxoid, which upon admin. neutralised antibody to the toxin.

Also claimed are: (1) a P.multocida type D strain 4677 bacterin with a cell-bound toxoid, which on admin. to an animal induced the prodn. of neutralising antitoxin; (2) a vaccine compsn. comprising the bacterin of (1) and a P.multocida soluble free toxoid; and (3) a vaccine compsn. comprising the components of (2) and a Bordetella bronchiseptica bacterin and an Arysipelothrix rhusiopathiae bacterin.

The vaccine is pref. produced by treating P. multocida in the exponential phase of growth with formaldehyde to inactivate the intracellular toxin. The vaccine dosage comprises 0.5-3 ml of a sterile suspension of an immunogenic amt. of the P. multocida bacterin with cell-bound toxoid, esp. 150 relative toxoid units/ml free toxoid. The vaccine also comprises an adjuvant, pref. Al(OH)4, a saponin, Mg(OH)2, Al phosphate, Mg phosphate or a Ca cpd.

USE/ADVANTAGE - The vaccines are used to vaccinate animals against atropic rhinitis and erysipelas. The vaccine is storage stable at 4 deg.C for at least 24 hours. Free and cell-bound toxoids have been seen to act synergistically in a single prepn. Other vaccine components include E. coli, pneumonic P. multocida, Streptococcus suis, Actinobacillus pleuropneumoniae, Clostridium perfringens C and D toxoids, pseudorabies virus (modified live and/or killed virus), rotavirus vaccine (modified live), coronavirus vaccine (modified live virus) and M. hyopneumoniae. Swine are pref. vaccinated at 1 week of age, with a booster dose at weaning age. Pregnant dams are given 2 doses, with the last given 2 weeks before farrowing. Booster doses are given prior to each subsequent farrowindy Dwg.0/0

FS CPI

FA AB

MC CPI: **B02-V02**; **C02-V02**; **D05-H07** ABEQ US 5695769 A UPAB: 19980126

Vaccine compsn. comprises a Pasteurella multocida type D strain 4677 bacterin with a cell-bound toxoid, which upon admin. neutralised antibody to the toxin.

Also claimed are: (1) a P.multocida type D strain 4677 bacterin with

a cell-bound toxoid, which on admin. to an animal induced the prodn. of neutralising antitoxin; (2) a vaccine compsn. comprising the bacterin of (1) and a P.multocida soluble free toxoid; and (3) a vaccine compsn. comprising the components of (2) and a Bordetella bronchiseptica bacterin and an Arysipelothrix rhusiopathiae bacterin.

The vaccine is pref. produced by treating P. multocida in the exponential phase of growth with formaldehyde to inactivate the intracellular toxin. The vaccine dosage comprises 0.5-3 ml of a sterile suspension of an immunogenic amt. of the P. multocida bacterin with cell-bound toxoid, esp. 150 relative toxoid units/ml free toxoid. The vaccine also comprises an adjuvant, pref. Al(OH)4, a saponin, Mg (OH) 2, Al phosphate, Mg phosphate or a Ca cpd..

USE/ADVANTAGE - The vaccines are used to vaccinate animals against atropic rhinitis and erysipelas. The vaccine is storage stable at 4 deg.C for at least 24 hours. Free and cell-bound toxoids have been seen to act synergistically in a single prepn. Other vaccine components include E. coli, pneumonic P. multocida, Streptococcus suis, Actinobacillus pleuropneumoniae, Clostridium perfringens C and D toxoids, pseudorabies virus (modified live and/or killed virus), rotavirus vaccine (modified live), coronavirus vaccine (modified live virus) and M. hyopneumoniae. Swine are pref. vaccinated at 1 week of age, with a booster dose at weaning age. Pregnant dams are given 2 doses, with the last given 2 weeks before farrowing. Booster doses are given prior to each subsequent farrowindy Dwg.0/0

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1992-056681 [07] WPIX

DNC C1992-025564

Controlled-density carriers for active substances - comprising high-ΤI and/or low-density particles and binder.

DC A96 A97 B07 C07 D13 D15 D16

BOG-HANSEN, T C; LIHME, A O F; NIELSEN, C S; NEILSEN, C S; LIHME, A; B IN G-HANSEN, T C; NIELSEN, C; LIHME, A O; BOEG-HANSEN, T C; BOGHANSEN, T C; BOG HANSEN, T C

PA(KEME-N) KEM ENTEC AS; (UPFR-N) UPFRONT CHROMOTOGRAPHY AS; (UPFR-N) UPFRONT CHROMATOGRAPHY AS; (KEME-N) KEM-EN-TEC AS; (KEME-N) KEMEN-TEC A/S CYC 36

WO 9200799 A 19920123 (199207)* PΤ

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B01J002-00

B01J002-00 AU 9182195 A 19920204 (199220) B01J002-00 98p EP 538350 A1 19930428 (199317) EN R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE G01N030-48 EP 607998 A2 19940727 (199429) EN

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B01J013-02 JP 06505911 W 19940707 (199431) B01J002-00 HU 67261 T 19950328 (199518) AU 659090 B 19950511 (199527) B01J002-00 EP 607998 A3 19940831 (199531)

B01J008-20 EP 722771 A1 19960724 (199634) ΕN R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

29p G01N030-48 EP 607998 B1 19960918 (199642) EN

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B01J002-00 EP 538350 B1 19960925 (199643) EN 39p

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T3 19970301 (199716) ES 2095944

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B01D015-08
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                  A 19990810 (199938)
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     19980108; CA 2086752 C CA 1991-2086752 19910708, WO 1991-DK195 19910708;
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FDT AU 9182195 A Based on WO 9200799; EP 538350 Al Based on WO 9200799; JP
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     JP 3168206 B2 Previous Publ. JP 06505911, Based on WO 9200799
PRAI DK 1990-1650
                      19900709
    2.Jnl.Ref; EP 175568; EP 21267; EP 25309; EP 74221; EP 7783; EP 88404; JP
     01047320; JP 59062339; SE 397669; WO 8102844; WO 8707851; WO 9014157;
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ICA B01D039-14; B01J002-08; C07B063-00 AΒ

9200799 A UPAB: 19931006

Compsns. for use as carriers for an active substance in a fluid and having controlled density relative to the fluid comprise high- and/or low density particles and a binder.

Examples describe: (a) hollow glass beads (HGB) bound with agarose, polyacrylamide, gelatin, agar-gelatin or chitosan; (b) HGB bound with gelatin contg. immobilised horseradish peroxidase (e.g. for waste water treatment) or yeast cells; (c) agarose-bound HGB activated with divinyl sulphone and mercaptoethanol for separating immunoglobulins from blood; (d) prods. of type (c) coupled to rabbit Ig for immunosorption of anti-Ig antibodies; (e) HGB bound with crosslinked acrylamide/acrylic acid copolymer for use as a cation exchanger, e.g. for treating waste water from the fish industry; (f) prods. of type (c) coupled to glucose oxidase; (q) prods. of type (c) coupled to N-acetylglucosamine for sepn. of wheat germ agglutinin; (h) solid glass beads bound with crosslinked acrylamide/acrylic acid copolymer or gelatin.

USE - The compsns. may be used 'as a solid phase matrix, carrier, or substrate material in a fluid bed reactor; or in a batch reactor; as a carrier of substances for sustained release; as a food material, medical, and vaccine for fish, or other animals living in water; as a material for treating waste water and m polluted waters; and as a material for treating polluted water such as oil polluted sea water' (sic).

0/7

CPI FS

FA AB; DCN

CPI: A12-V01; B04-B02C2; B04-B04A6; B04-B04C6; B04-C02D; B04-C02E3; MC B04-C03B; B04-D02; B07-A02; B10-A10; B10-E03; B12-M10A; C04-B02C2; C04-B04A6; C04-B04C6; C04-C02D; C04-C02E3; C04-C03B; C04-D02; C07-A02; C10-A10; C10-E03; C12-M10A; D03-G; D03-H01; D04-A01; D05-A01; D05-A01B1; D05-A03A; D05-H07; D05-H10

ABEQ EP 538350 A UPAB: 19931025

Compsns. for use as carriers for an active substance in a fluid and having controlled density relative to the fluid comprise high- and/or low density particles and a binder.

Examples describe: (a) hollow glass beads (HGB) bound with agarose, polyacrylamide, gelatin, agar-gelatin or chitosan; (b) HGB activated with divinyl sulphone and mercaptoethanol for sepg. immunoglobulins from blood; (d) prods. of type (c) coupled to rabbit Ig for immunosorption of anti-Ig antibodies; (e) HGB bound with crosslinked acrylamide/acrylic acid copolymer for use as a cation exchanger, e.g. for treating waste water from the fish industry; (f) prods. of type (c) coupled to glucose oxidase; (g) prods. of type (c) coupled to N-acetylglucosamine for sepn. of wheat germ agglutinin; (h) solid glass beads bound with crosslinked acrylamide/acrylic acid copolymer or gelatin.

USE - Useful as a solid phase matrix, carrier, or substrate material in a fluid bed reactor; or in a batch reactor; as a carrier of substances for sustained release; as a food material, medical, and vaccine for fish, or other animals living in water; as a material for treating waste water and polluted waters; and as a material for treating polluted water such as 'oil polluted sea water' (sic). Dwg.0/7

607998 B UPAB: 19961021 ABEQ EP

Chromatographic adsorbent particles having covalently bound at least one active substance for binding molecules in liq. chromatographic fluid bed process and controlled particle size, is characterised in (a) that porous composite material consists of conglomerate having controlled relative density and comprising: (i) at least two density-controlling basic particles of amorphous silica, quartz, or glass having low density particles; and (ii) matrix formed by consolidating at least one conglomerating agent selected from natural and synthetic polysaccharides and other carbohydrate based polymers and having at least one active substance is covalently bound. Density and size range are selected to

provide desired floatation/sedimentation properties of adsorbent particles in liquid. $\ensuremath{\text{Dwg.0/6}}$

538350 B UPAB: 19961025 ABEQ EP Chromatographic absorbent particles having covalently bound at least one active substance for binding molecules in a liquid chromatographic fluid bed process; said adsorbent particles being constituted by a porous composite material having pores allowing access to the interior of the composite material of said molecules; characterized in (a) that the porous composite material consists of a conglomerate having controlled density; said conglomerate consisting of: (i) at least two density controlling particles selected from the group consisting of low density particles having a density providing floatation and high density particles having a density providing sedimentation of the conglomerate in said liquid; and (ii) a matrix formed by consolidating at least one conglomerating agent selected from the group consisting of natural and synthetic organic monomers and polymers; said at least two density controlling particles being dispersed in said matrix; (b) that the size range of the adsorbent particles is controlled; (c) that said density and said size range are selected to provide desired floatation/sedimentation properties of said adsorbent particles in the liquid in said fluid bed process; and (d) that the at least one active substance is covalently bound to said matrix; with the proviso that when said at least two density controlling particles are of amorphous silica, quartz, or glass, than said conglomerating agent does not consist of natural and synthetic polysaccharides and other carbohydrate based polymers.

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(C) 2003 THOMSON DERWENT
L118 ANSWER 14 OF 14 WPIX
    1984-056355 [10] WPIX
AN
DNC C1984-023932
    Prodn. of vaccine for treating tick paralysis - by
TI
     detoxification of purified tick salivary gland extract.
DC
    B04 C03
ΙN
    STONE, B
     (CSIR) COMMONWEALTH SCI & IND RES ORG
PΑ
CYC 1
PΤ
    AU 8316459
                  A 19840119 (198410)*
                                              23p
ADT AU 8316459 A AU 1983-16459 19830630
                                                 19830630
PRAI AU 1982-4813
                      19820712; AU 1983-16459
    A61K035-64; A61K039-00; C07G007-00
IC
AΒ
         8316459 A UPAB: 19930925
    ΑU
    The prodn. comprises (1) obtd. a tick salivary gland extract; (2) purifn.
    of the extract by centrifugation or filtration to give a purified
     fraction; (3) addn. of a detoxifying agent (I) to the fraction (opt. after
    purification or modification); and (4) addn. of an adjuvant
     (II).
```

Also claimed are prodn. of an antiserum comprises injection into an animal of the purified fraction obtd. in step (2), opt. after further purification or modification, and the antiserum is subsequently recovered, and prodn. of a toxin comprises treatment of the purified fraction obtd. in step (2), opt. after further purification or modification, with a gel contg. Al(OH)3 or Mg(OH)

2 to bind non-toxic material, and the toxin fraction is sepd. The vaccines protect domestic pets and livestock against paralysis by ticks, esp. by Ixodes holocyclus. The antitoxin has high potency and may be used to treat tick paralysis in humans.

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0/0
FS CPI
FA AB
MC CPI: B02-V; C02-V
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Dwq.0/7

=> d his

L35

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                E DK2000-1194/AP, PRN
              1 S E4
L1
     FILE 'REGISTRY' ENTERED AT 15:18:24 ON 24 APR 2003
L2
              1 S 1309-42-8
              1 S 13463-67-7
L3
L4
              1 S 61042-72-6
            187 S 463-79-6/CRN AND MG/ELS
L5
             31 S L5 AND H2O
L6
             11 S L6 AND 3/NC
L7
              8 S L7 NOT MNS/CI
L8
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L9
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L10
L11
         112281 S L3
         197480 S (TI OR TITANIUM)()(DIOXIDE OR OXIDE) OR TIO2 OR TITANIA
L12
             14 S L4
L13
L14
            125 S L8
L15
              7 S (MG OR MAGNESIUM) () CARBONATE() (5H2O OR PENTAHYDRATE)
     FILE 'REGISTRY' ENTERED AT 15:23:37 ON 24 APR 2003
              3 S L5 AND 2/NC NOT (IDS OR MNS)/CI
L16
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L17
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L18
         234093 S L9-L15,L17-L18
L19
             1 S L1 AND L19
L20
                E SONI N/AU
L21
             57 S E3, E5, E11
                E KRISTENSEN/AU
                E KRISTENSEN N/AU
L22
              4 S E3, E8, E12
                E RAHBEK J/AU
              2 S E4
L23
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                E AASMUL OLSEN/AU
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L24
                E LUND L/AU
L25
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L26
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L28
L29
              2 S E37, E38
                E ABELLO/PA, CS
L30
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L31
              1 S L20, L30
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L33
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L34
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8768 S E14, E15, E77-E84, E92, E96, E143-E145, E172

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             47 S L19 AND L35
L41
             10 S L19 AND L37
L42
            500 S L19 AND L36
L43
             29 S L38-L43 AND VACCIN?
L44
             27 S L19 AND PARENTER?
L45
             15 S L45 AND L38-L43
L46
             53 S L44-L46
L47
                E ADJUVANT/CT
L48
            561 S E6, E8, E10
                E E6+ALL
           5058 S E2
L49
             14 S L19 AND L48-L49
L50
            108 S L19 AND ADJUVANT
L51
             12 S L50, L51 AND L47
L52
             30 S L47, L51 AND VACCIN?
L53
L54
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L56
             14 S L1, L31, L54, L56
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             12 S L58 AND (CPLA2 OR LIQUID COMPOSITION OR IMMUNE RESPONSE OR TA
L59
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L62
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L63
                E PLG/CN
L64
              2 S E3
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                E PLGA/CN
                E PLG A/CN
              1 S E7,E8
L66
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L67
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L68
              3 S PLGA()(5010 OR 5020)
L69
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L70
          11048 S (GLYCOLIC OR POLYGLYCOLIC OR POLY GLYCOLIC) (.) ACID
L71
L72
           4145 S L70 AND L71
L73
            439 S L67 AND L68, L69
L74
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           1553 S GLYCOLIDE(S) LACTIDE(S) COPOLYMER
L75
L76
           1168 S POLY(2W)LACTIDE CO GLYCOLIDE
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L80
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L81
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             33 S L80 AND L32-L37
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L84
             55 S L81-L83
L85
             6 S L84 AND L61
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L86
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              9 S E10-E18
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              0 S L15/BIX
L94
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           5384 S E2 OR 1509/DRN
                E TITANIUM DIOXIDE/DCN
                E E3+ALL
L96
          33296 S E2 OR 1966/DRN
                E MAGNESIUM CARBONATE/DCN
                E E3+ALL
           3901 S E2 OR 1359/DRN
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L98
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L99
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L110
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             14 S L103, L112
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L114
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L115
              4 S L114 AND INJECT?/BIX
L116
              5 S L114 AND PARENTER?/BIX
L117
L118
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